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NOTICES

With this issue of the JOURNAL there appear two new names on the Advisory Editorial Board, Dr. Edward D. Churchill of Boston and Dr. Stuart W. Harrington of Rochester, Minn. Also, the Associate Editorship has been reorganized. Dr. Duff S. Allen, who has served as Associate Editor since the founding of the JOURNAL, has found it necessary to resign, and his resignation has been accepted with sincere regret. In his place, Dr. Brian Blades of St. Louis, and *ex officio,* the Secretary of the American Association for Thoracic Surgery, Dr. Richard H. Meade of Philadelphia, have been appointed as Associate Editors.

In the last three issues of the JOURNAL some advertisements of World Peaceways, Inc., have appeared. The editorial board was not consulted about the acceptance of this material, and it regrets very much that space was allotted for propaganda purposes. It is a pleasure, however, to announce that no more advertising from World Peaceways, Inc., or from any other propaganda organization will appear in the JOURNAL.

The Editor

Original Communications

SULFANILAMIDE AND EXPERIMENTAL TUBERCULOSIS IN THE GUINEA PIG*

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IN TWO previous communications we drew attention to the inhibitory effect of sulfanilamide upon the growth of acid-fast bacilli in vitro. Reference was also made elsewhere to the effect of sulfanilamide upon the development of experimental tuberculosis in the guinea pig. We are here concerned with the effect of varying doses of sulfanilamide given at stated intervals, upon the development of experimental tuberculosis in guinea pigs of specified weights, first treated three, ten, and sixteen days after infection. In these experiments seventy-two animals were treated; fifty-one were kept as controls. The results of a preliminary investigation dealing with the effect of sulfanilamide upon guinea pigs infected with virulent bovine tubercle bacilli (B_1 Saranac Lake) will also be reported. In this series eight guinea pigs were treated three and ten days after infection; eight were kept as controls.

The gross and microscopic findings in our experiments will be described in detail.

Before referring to our experiments, mention will be made of the published works of others.

REVIEW OF LITERATURE

Rich and Follis infected fifty-nine guinea pigs, weighing on the average 400 Gm., subcutaneously with 0.1 c.c. of a suspension of virulent human tubercle bacilli. This suspension contained, on an average, five bacilli per oil immersion field. Rich and Follis started *treatment three days before infection and on the day of infection.* The drug was deposited in the cheek pouches of their animals which were treated daily for periods of five, and in some instances six, weeks. Rich and Follis found that, when the daily dose of sulfanilamide was 100 mg., no appreciable macroscopic or microscopic difference could be discerned between the ten treated animals and the seven controls. Two hundred milligrams of the drug daily (100×2) produced a definite inhibitory effect. This was evidenced by the fact that, whereas tubercles were found microscopically in the tissues of all treated animals, their number and extent were markedly less in this group of six animals than in a similar control group. In addition, in the case of treated animals, macroscopic lesions were observed in the spleen in only one instance.

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When Rich and Follis increased the dose of the drug to 500 mg. daily (100 mg. at 9 A.M., 2 P.M., and 6 P.M., and 200 mg. at 11 P.M.), a striking difference was noted. All fifteen untreated animals had large local lesions, enlarged regionary lymph nodes, and at necropsy in the fifth and sixth weeks, they showed greatly enlarged tuberculous tracheobronchial nodes and spleens. The local lesions and regionary nodes of treated animals coming to necropsy in the fifth week were minute in comparison. Treated animals did not show any splenic enlargement and remarkably minute tracheobronchial nodes. Rich and Follis stated that in none of the treated animals did the drug completely prevent the growth of the bacilli. They regarded 500 mg. sulfanilamide daily as too large a dose, for nine of fifteen treated animals died as a result of overdosage.

Smithburn infected twenty guinea pigs weighing from 344 to 350 Gm. intracerebrally with 0.00001 mg. moist weight of human tubercle bacilli. Treatment with prontylin was started twenty-four hours after infection. Ten animals were given 200 mg. of prontylin in 10 c.c. of saline, intra-abdominally by injection, for twenty-three days. The single daily dose was then increased to 250 mg. for an additional seven days. Gross necropsy findings were similar in both treated and untreated controls. There was no appreciable difference in the survival time of both groups.

Buttle and Parish infected twenty guinea pigs subcutaneously with 0.5 mg. of virulent human tubercle bacilli, and twenty with 0.05 mg. of the same strain. A similar number of 400-Gm. guinea pigs were infected with 0.1 mg. of bovine tubercle bacilli, and twenty with 0.01 mg. of the same strain. Half the number of animals in each group were kept as controls. Buttle and Parish started treatment on the day of infection. They employed a 50 per cent suspension of sulfanilamide in 5 per cent gum arabic. The suspension was ejected from a syringe at the back of the animal's tongue and pharynx. Daily treatments with 500 mg. of sulfanilamide (100 mg. given at 9 A.M., 200 mg. at 1:30 P.M., and 200 mg. at 10 P.M.) were given at the start. After five days of treatment the 500-mg. daily dose was found to be too toxic and was therefore reduced to 250 mg. daily. This dose of sulfanilamide was administered daily for thirty-seven days. A slight inhibitory effect was observed in treated guinea pigs infected with human tubercle bacilli. This inhibitory effect was less marked in the case of guinea pigs infected with bovine tubercle bacilli. The tuberculous lesions of all treated animals appeared less extensive than those noted in the untreated controls. Rabbits infected with bovine tubercle bacilli and treated with sulfanilamide failed to reveal any differences when compared with the untreated infected control animals.

Greey, Campbell, and Culley infected forty-eight, 350-Gm. guinea pigs subcutaneously with 0.2 c.c. of a suspension which showed from two to six bacilli per oil immersion field. Treatment was started three days before infection and seventeen and twenty-four days after infection. Sulfanilamide was administered orally in daily amounts of 300 mg. given in three equally divided doses at 9 A.M., 5 P.M., and 11 P.M. Animals first treated three days before infection showed fewer and smaller lesions in their spleens and lungs than did the control animals. When treatment was started seventeen and twenty-four days after infection, no appreciable macroscopic difference could be noted between treated and control animals. Microscopically, however, tuberculous lesions of all treated animals showed fewer bacilli, less necrosis, and a greater proliferation of endothelial cells. The control animals survived longer than the treated animals. Greey, Campbell, and Culley regarded a daily dose of 300 mg. of sulfanilamide as toxic for their 350-Gm. animals. More recently, Greey, Boddington, and Little reported the results of treatment of forty guinea pigs, weighing, on the average, 350 Gm., with 300 mg. each of five different sulfonamide compounds (sulfanilamide, diacetyl sulfone, uleron, septazine, and 50 mg. of prontosil base and 2 c.c. of 2.5 per cent solution

of neoprontosil). Eight guinea pigs, four treated and four controls, were used for each compound. Treatment was started three days before subcutaneous infection with 0.2 c.c. of a suspension of human tubercle bacilli containing from two to six organisms per oil immersion field. The macroscopic lesions of animals treated with sulfanilamide were found to be small and few in number. They were multiple and prominent in the controls. Half of their animals died before the end of the fourth week; consequently, the dose of sulfanilamide was decreased. None of the other compounds referred to produced any inhibitory effect. Greey and his associates also infected rabbits weighing, on the average, 1.2 kg. with bovine tubercle bacilli. These animals were given 200 mg. daily of the above-mentioned compounds. The dose of prontosil soluble was increased to 8 c.c. of a 2.5 per cent solution. All rabbits died within four weeks after infection and showed generalized tuberculosis. No difference was observed between treated and untreated control animals.

Kolmer, Raiziss, and Rule infected sixteen guinea pigs subcutaneously with 0.00002 Gm. of virulent tubercle bacilli. Treatment with sulfanilamide which was given intramuscularly was begun two hours after infection. Four animals received 0.2 Gm. of sulfanilamide per kilogram divided into two doses given six hours apart daily for eight days. Four animals received 0.3 Gm. of sulfanilamide per kilogram, and four animals received 0.5 Gm. of the drug per kilogram given in two doses. Four animals were kept as controls. Kolmer and his co-workers interpreted their results "as indicating that sulfanilamide had no curative activity under the conditions of the experiment." They also stated that "six derivatives of sulfanilamide in the form of their sodium salts, by intramuscular injection were without demonstrable curative effects in the treatment of experimental tuberculosis of guinea pigs, when treatment was started nine days after inoculation."

Dietrich infected eight guinea pigs with 0.5 c.c. of a suspension of tubercle bacilli. He treated these animals with a 2.5 per cent solution of prontosil given intraperitoneally daily in doses of 100 mg. per kilogram of body weight. No favorable influence of the drug on the infection was observed. The treated animals died sooner than did the control animals.

Feldman and Hinshaw reported upon the effect of sulfapyridine on experimental tuberculosis in the guinea pig. Twenty animals were treated, and twenty were kept as controls. Each guinea pig was infected subcutaneously over the sternum with 0.0001 mg. of a strain of *Mycobacterium tuberculosis* var. hominis. The strain of tubercle bacilli employed had been isolated three months previously from sputum. The experiment was continued for eight weeks. Treatment was started three days previous to infection. Two hundred and fifty milligrams of sulfapyridine were given twice daily for ten days. The dose was then reduced to 125 mg. given twice daily. With few exceptions, the controls not only maintained, but actually increased, their weight. This was in striking contrast to the marked loss of weight of treated animals. Feldman and Hinshaw concluded that, under the conditions of their experiments, "sulfapyridine exerts a definite and striking modification and retardation of the expected course of experimental tuberculosis in guinea pigs."

Birkhaug infected forty-eight guinea pigs in the leg with 0.00001 mg. of virulent bovine tubercle bacilli. Treatment of twenty-four guinea pigs with 0.2 c.c. of "prontosil soluble Bayer" (disodium-sulfonamide-benzolazo-acetylamine-oxy-naphthalene-disulfonate) was begun seven days before infection. Treatment after infection was continued as follows: 0.2 c.c. for four weeks; 0.3 c.c. for two weeks; 0.5 c.c. for eight weeks; and 1 c.c. for nine weeks. The total dosage for the twenty-two-week period was 99.4 c.c. of prontosil soluble (2,485 mg. of sulfonamide). Birkhaug concluded that the preparation of sulfonamide which had been employed had clearly inhibited the tuberculous process in the lymph nodes and

in the viscera. The microscopic findings were in keeping with the gross findings. The treated animals not only showed less tuberculosis than the controls, but also a gain in weight; the control animals showed a loss in weight.

Nils Levin recently reported upon the effect of streptal soluble (sulfanilamide) and experimental bovine tuberculosis in the guinea pig. Sixteen guinea pigs weighing between 250 and 300 Gm. were employed for the experiment. All animals received a prophylactic dose of streptal for eight days. Half the animals received 0.15 Gm. daily, and the remainder, 0.015 Gm. On the eighth day all the animals were infected with 0.05 mg. of tubercle bacilli (Löffler-Vallé). Half the animals were then kept as controls; the remainder were treated for short periods. Levin concluded that the prophylactic use of streptal was without inhibitory effect upon the development of experimental tuberculosis in the guinea pig.

Steinbach and Dillon subcutaneously infected fifty-four guinea pigs, averaging 365 Gm. in weight, with 0.0001 mg. of virulent bovine tubercle bacilli (B_1). Forty-two animals were treated. Fourteen guinea pigs received 100 mg. of sulfanilamide daily; a similar group received 200 mg., and the remaining group, 300 mg., of sulfanilamide (100×3) daily. One-half the animals in each group were treated by os, and the remaining half, by subcutaneous injection. Twelve other animals were treated for three days with sulfanilamide in 100-mg. doses administered orally three times daily. These guinea pigs were then infected as noted above. Sulfanilamide treatments were continued throughout the course of the experiment. Steinbach and Dillon concluded that "sulfanilamide treatment initiated on the day of infection and maintained throughout the experiment failed to affect the course of experimental tuberculosis in the guinea pig. Guinea pigs treated with sulfanilamide before the infection and treated daily thereafter showed no evidence of being benefited by the drug."

The fifty-nine guinea pigs in our first published experiments weighed, on an average, 350 Gm. We started treatment five and ten days after infection. Under the conditions of the experiments, our results were similar to those of Rich and Follis, who started treatment three days before infection and on the day of infection. Daily treatment doses of from 340 to 380 mg. of sulfanilamide given in four divided doses proved adequate, yet not very toxic, for most guinea pigs weighing 350 Gm. In this preliminary report we drew attention to the fact that an inhibitory effect is possible even though treatment is interrupted at intervals.

EXPERIMENTS

One hundred and twenty-three guinea pigs were infected subcutaneously with virulent human tubercle bacilli. The animals were divided into nine groups because of variations in weight and because of differences in the daily and total amounts of sulfanilamide given. These nine groups of animals represent two separate sets of experiments carried out consecutively. In the first five experiments (Series 1 to 5, inclusive), a 3-week-old culture of virulent human tubercle bacilli was employed; in the second set of experiments (Series 6 to 9, inclusive), a 4-week-old culture was employed. Both strains were isolated directly from sputum. In each instance a suspension was prepared by triturating and suspending the tubercle bacilli in a buffer solution (Clark and Lubs series) pH 8.0. In order to avoid large clumps, the suspensions were filtered through two layers of Whatman paper No. 2. The final suspensions were diluted so as to show on smear one bacillus per oil immersion field. The infective dose uniform for all animals in a particular group varied from 1.0 to 1.4 c.c. The sulfanilamide (prontylin) was given orally in gelatin capsules (Parke, Davis & Co., Nos. 3, 4, and 5). The capsules were dipped in a solution of glucose in tepid water to facilitate swallowing. The capsules were forced down by

TABLE I

	NO.	WEIGHT		NO. DAYS TREATED	AVERAGE TREATMENT DOSE (MG.)	TOTAL DOSE (MG.)	AVERAGE DAILY DOSE (MG.)	D.	S.	DEGREE MACROSCOPIC TUBERCULOSIS			SIZE OF SPLEEN (MM.)
		B.I.	P.M.							SPLEEN	LIVER	LUNGS	
Series 1 (Average Weight, 310 Gm.)													
Treated 10 days after infection	1	300	367	20	429	8,580	220		50	++	+	+	31×14
	2	310	407	20	429	8,580	220		50	+	+	++	31×16
	3	325	476	20	429	8,580	220		50	+	±	±	32×12
Treated 16 days after infection	9	310	372	15	420	6,300	162		50	++	+++	+	45×18
	10	305	396	9	420	3,780	97		50	+++	+++	+++	50×20
Controls	11	305	310						50	+++	++++	+++	41×19
	12	310	340						50	+++	+++	+++	40×20
	13	305	317						50	++++	++++	+++	52×22
	14	315	451						50	++	+	++++	40×18
	15	325	453						50	+++	+++	+++	40×15
Series 2 (Average Weight, 335 Gm.)													
Treated 10 days after infection	16	340	409	20	480	9,600	246		50	±	±	±	28×14
	17	335	431	20	480	9,600	246		50	±	±	±	23×11
	18	335	365	14	480	6,720	172		50	+	+	+	26×11
Controls	19	335	428						50	+++	+++	+++	48×25
	20	335	431						50	++	+++	+	40×17
	21	340	479						50	+++	++++	+++	59×22

B.I. = weight before infection.
P.M. = weight at necropsy.
D. = died, number of days.
S. = sacrificed, number of days.
±, questionable; +, slight; ++, moderate; +++, extensive; ++++, very heavy infection.

means of an applicator, and a small quantity of the glucose was again given to each animal. Treatment was interrupted for stated intervals when an animal showed a loss in weight, or in anticipation of toxic signs. In all experiments the total daily amount of sulfanilamide was divided into four doses given at 7 A.M., 12 noon, 6 P.M., and 11:30 P.M. The diet given all animals consisted of water for two hours immediately following the administration of the drug at 7 A.M. At 10 A.M. rolled oats were also given, and immediately following the 12 noon capsule, each guinea pig received 1 oz. of lettuce. At 4 P.M. full grain oats were given. After the 6 P.M. treatment, each animal received fresh carrots, and after the 11:30 P.M. treatment, hay.

The duration of Experiments 1 to 5, inclusive, was fifty days. In all other experiments, unless otherwise stated, the experiments were terminated thirty-five days after infection. Inadequately treated animals which died early in the course of an experiment are referred to in the text, but not in the tables.

SERIES 1

Fifteen guinea pigs weighing, on the average, 310 Gm. were infected subcutaneously with 1 c.c. of the bacillary suspension. Five were kept as controls. Eight were first treated ten days after infection, and two, sixteen days after infection. The former were given 480 mg. (105, 105, 105, 165) of sulfanilamide on the 11th, 12th, and 13th days after infection. Two guinea pigs (Nos. 6 and 7), died on the 14th day. Both had been treated for only three days and had received only 1,440 mg. of sulfanilamide. Guinea pig 8 received three daily doses of 480 mg. each and died on the 16th day. Four hundred and twenty milligrams (105×4) of sulfanilamide were given to the remaining animals on the 16th, 17th, 19th, 20th, 22nd, 23rd, and 25th days after infection. Two animals (Nos. 4 and 5), after receiving 3,960 mg. of sulfanilamide on nine treatment days, died on the 25th day. Animal No. 4 showed a slight degree of macroscopic tuberculosis in both the spleen and liver. All other animals which died during the course of the experiment were free of macroscopic tuberculosis. The three treated animals which now remained were given 420 mg. of the drug on the 31st, 32nd, 34th, 35th, 38th, 39th, 43rd, 44th, 48th, and 49th days after infection. They were sacrificed with the controls, fifty days after infection. The two animals first treated sixteen days after infection were also sacrificed on this date.

COMMENT

The local lesions of treated animals were smaller and less necrotic than those of the controls. The regionary lymph nodes of treated animals were smaller, too. The three animals treated ten days after infection and referred to in Table I showed less tuberculosis than the controls. Animals 1 and 2 showed more tuberculosis than Animal 3 which showed a greater gain in weight. Compare the results of this series referred to in Table I with those of Series 6. (Table I.)

SERIES 2

Six guinea pigs weighing, on the average 335 gm. were infected with 1.1 c.c. of the suspension. Three were treated and three were kept as controls. Two animals received 480 mg. of sulfanilamide on the 11th, 12th, 13th, 16th, 17th, 19th, 20th, 22nd, 23rd, 25th, 31st, 32nd, 34th, 35th, 38th, 39th, 43rd, 44th, 48th, and 49th days after infection. There were thus twenty treatment days and an equal number of days when sulfanilamide was not given. Because it failed to maintain its weight

until treatment was interrupted for a considerable period, Animal 18 received only fourteen daily treatments. All animals survived the experiment and were sacrificed fifty days after infection (Fig. 1 and Table I).

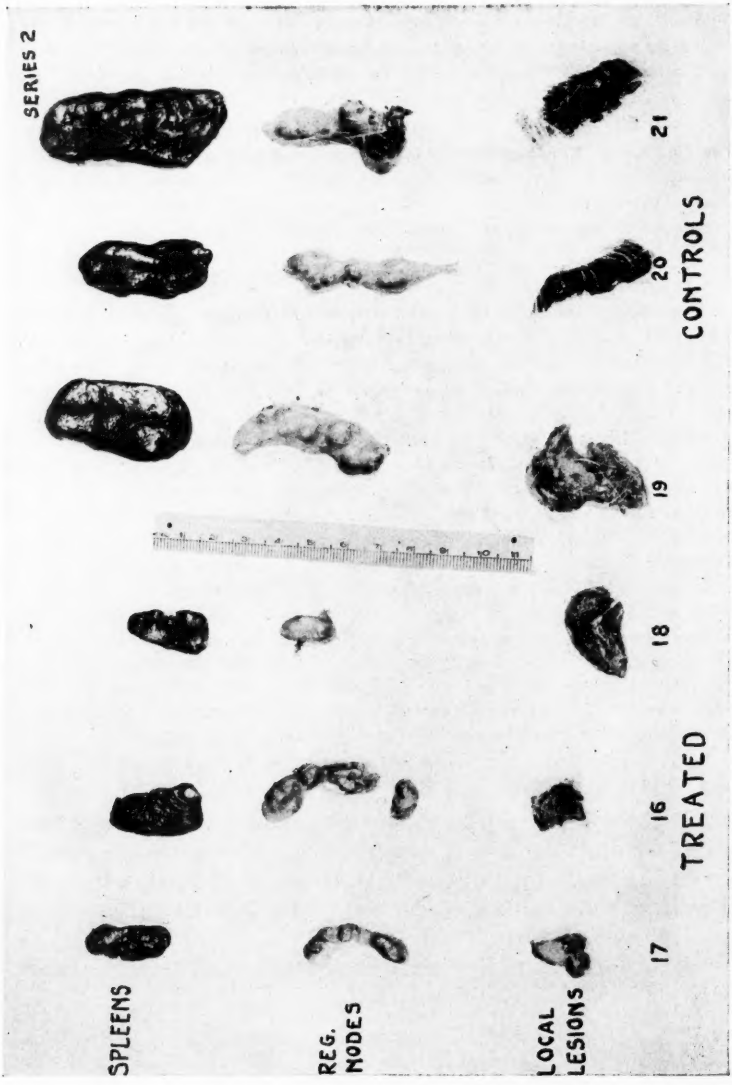

Fig. 1.—Series 2. This figure shows the spleens, regionary inguinal nodes, and local lesions of three treated animals (Nos. 17, 16, and 18) and three control animals (Nos. 19, 20, and 21). See the text and Table I for further details.

COMMENT

The drug at no time depressed the weight curve of Animals 16 and 17 of this series. The local lesions and regionary lymph nodes of the three treated animals were definitely smaller and less necrotic than

those of the controls. The spleens of the treated animals were normal in size; the spleens, livers, and lungs in two animals (16 and 17) showed questionable macroscopic lesions. The untreated control animals, on the other hand, showed not only enlarged spleens, but also numerous and extensive macroscopic tuberculous lesions in the spleen, liver, and lungs. Compare Series 2 with Series 7.

SERIES 3

Fifteen guinea pigs weighing, on the average, 365 Gm. were infected with 1.2 c.c. of the suspension. Four animals were kept as controls; eight were treated ten days after infection, and three, sixteen days after infection. Animals 22, 23, and 24 received 480 mg. of sulfanilamide on the 11th, 12th, 13th, 16th, 17th, 19th, 20th, 22nd, 23rd, 25th, 31st, 32nd, 34th, 35th, 38th, 39th, 43rd, 44th, 48th, and 49th days after infection. To Animals 25, 26, and 27, 480 mg. of the drug were given on the 11th, 12th, 13th, 17th, 18th, 20th, 21st, 23rd, 24th, 26th, 32nd, 33rd, 39th, 40th, 44th, and 45th days after infection. Animal 25, which gained in weight, received two additional daily treatments on the forty-eighth and forty-ninth days after infection.

The final weights which have been recorded are appreciably greater than what was noted on the thirty-third day after infection. Animal 26 barely maintained its weight; Animal 27 lost in weight. From the thirty-third day until the conclusion of the experiment, rest periods, when no drug was given, were prolonged. Animal 29, which died fifteen days after infection, was free of gross tuberculosis; Animal 28 was free on the forty-third day after infection.

The three animals (30, 31, and 32) first treated sixteen days after infection received 480 mg. of sulfanilamide on the 17th, 18th, 20th, 21st, 23rd, 24th, 26th, 32nd, and 33rd days after infection. Treatment was then stopped because one animal (No. 32) died on the thirty-third day after infection, and because the other two animals had lost in weight, in one instance, considerably.

COMMENT

With the exception of Animals 27 and 26, all animals in this series treated ten days after infection and referred to in Table II showed less tuberculosis than did the untreated controls.

SERIES 4

Ten guinea pigs weighing, on an average, 390 Gm. were infected with 1.3 c.c. of the suspension. Five animals were kept as controls. Five received 420 mg. of sulfanilamide on the 11th, 12th, and 13th days after infection. Animal 41 died fifteen days after infection. Treatment of the remaining animals was started up again on the sixteenth day after infection when 420 mg. of sulfanilamide were given. On the seventeenth day the dose was increased to 480 mg. because the remaining treated animals appeared to tolerate the drug well. This dose was repeated on the 20th, 21st, 23rd, and 24th days after infection. Treatment of one animal which had lost considerably in weight was discontinued on the twenty-fourth day. This animal (No. 40) died forty-five days after infection. The three remaining animals (37, 38, and 39) received 480 mg. of sulfanilamide on the 27th, 33rd, 34th, 40th, 41st, 45th, 46th, 48th, and 49th days after infection. Control animal 46 died forty-two days after infection.

TABLE II

	NO.	WEIGHT		NO. DAYS TREATED	AVERAGE TREATMENT DOSE (MG.)	TOTAL DOSE (MG.)	AVERAGE DAILY DOSE (MG.)	D.	S.	DEGREE MACROSCOPIC TUBERCULOSIS			SIZE OF SPLEEN (MM.)
		B.I.	P.M.							SPLEEN	LIVER	LUNGS	
Series 3 (Average Weight, 365 Gm.)													
Treated 10 days after infection	22	360	356	20	480	9,600	246		50	+	+	+	34×16
	23	355	402	20	480	9,600	246		50	+	+	+	41×21
	24	375	485	20	480	9,600	246		50	+	++	+	40×16
	25	370	412	18	480	8,640	222		50	++	±	+	38×15
	26	350	350	16	480	7,680	197		50	+++	+	+	38×17
	27	362	320	16	480	7,680	197		50	+++	++	+	38×16
	28	365	245	10	480	4,800	145	40		+	+	+	35×17
Treated 16 days after infection	30	350	297	9	480	4,320	111		50	+++	++++	+++	51×22
	31	365	355	9	480	4,320	111		50	+++	+++	+++	45×19
Controls	33	360	347						50	+++	+++	+++	53×25
	34	375	443						50	++	+++	+++	39×17
	35	355	592						50	+++	+	++	46×21
	36	370	598						50	+++	++++	++++	57×27
Series 4 (Average Weight, 390 Gm.)													
Treated 10 days after infection	37	380	383	18	466	8,400	215		50	+	+	+	31×16
	38	405	413	18	466	8,400	215		50	+++	+	+++	40×17
	39	390	477	18	466	8,400	215		50	++	+	++	40×20
	40	460	275	9	460	4,140	118	45		++++	++++	++++	56×32
Controls	42	405	402						50	+++	++++	++++	50×20
	43	380	410						50	++	+	++	40×20
	44	405	517						50	+++	+	+	53×25
	45	390	635						50	+++	++	+++	45×19
	46	380	275					42		++++	++++	+++	42×17
Series 5 (Average Weight, 420 Gm.)													
Treated 10 days after infection	47	425	572	20	600	12,000	308		50	+	+	±	31×19
	48	420	360	14	600	8,400	210	50		++	++	+	35×19
Controls	51	435	422						50	+++	+	+	46×23
	52	440	546						50	++	++	+	45×22
	53	445	608						50	+++	+	+++	40×21
	54	415	633						50	+++	+	++++	40×23

For explanation of abbreviations and symbols see footnotes to Table I.

COMMENT

Animal 29, which died fifteen days after infection, showed a slightly enlarged regionary lymph node. The guinea pig (No. 40) which received but little treatment because of loss in weight and which died forty-five days after infection showed a small, nonulcerated, local lesion and a small regionary node. The spleen of this animal was enlarged and contained numerous necrotic tubercles, as did the liver and lungs. This animal, on the whole, showed more tuberculosis than did the control animals. The control animal (No. 46) which died forty-two days after infection showed a small, slightly necrotic, local lesion; the regionary nodes of this animal were small, and the spleen was enlarged. It showed numerous and extensive necrotic tuberculous lesions, as did the liver and lungs. Only one animal (No. 37) in the treated group in this series was benefited. Compare Series 4 with Series 8.

SERIES 5

Eight guinea pigs weighing, on the average, 420 Gm. were infected with 1.4 c.c. of the suspension. Four animals were kept as controls, and four were treated. Treatment was started ten days after infection. Following three daily doses of 600 mg. of sulfanilamide, one animal died. On the 17th, 18th, 20th, 21st, 23rd, 24th, and 26th days after infection, 600 mg. of sulfanilamide were given to three remaining animals. Animal 49 died twenty-seven days after infection. Treatments with 600 mg. of the drug were again given to the two remaining animals on the 30th, 31st, 34th, and 35th days. Treatment of one animal (No. 48) was discontinued on the thirty-sixth day because it had lost in weight. Animal 47 received additional 600-mg. doses of the drug on the 38th, 39th, 43rd, 44th, 48th, and 49th days after infection.

COMMENT

The animal (No. 50) which died fourteen days after infection showed a small local lesion, small regionary inguinal lymph nodes, and, grossly, three small tubercles in the spleen. Animal 49, which died twenty-seven days after infection, had lost greatly in weight (from 425 to 310 Gm.). The regionary nodes of this animal were enlarged; the spleen, which was enlarged, showed multiple caseous tubercles, as did the liver. A few scattered tubercles were also present in the lung of this animal. Animal 47, which survived the experiment, and Animal 48, which died on the fiftieth day after infection, showed much less local and much less generalized tuberculosis than did the untreated control animals. (Table II.)

SERIES 6

Eighteen guinea pigs weighing, on the average, 310 Gm. were infected subcutaneously in the groin with 1 c.c. of the suspension. Six guinea pigs were kept as controls; six were first treated three days after infection, and six, ten days after infection. Four of the six animals first treated three days after infection received 420 mg. (105×4) of sulfanilamide on the 4th, 5th, 7th, 8th, 11th, 12th, 14th, 15th, 18th, 19th, 21st, 22nd, 25th, 26th, 29th, 30th, 33rd, and 34th days after infection. They were sacrificed with the controls on the thirty-fifth day after infection.

Animals 59 and 60 received only fourteen treatments because the former lost slightly in weight and because the latter lost weight appreciably. Both these animals were kept alive, with difficulty, to the conclusion of the experiment. The six animals in this series first treated ten days after infection received 480 mg. (105, 105, 105, 165) of the drug on the 11th, 12th, 14th, 15th, 18th, and 19th days after infection. Because the animals were barely maintaining their weight, the daily dose of sulfanilamide was reduced to 420 mg. (105×4). Further treatments were given on the 21st, 22nd, 25th, 26th, 29th, 30th, 33rd, and 34th days after infection. Two treated animals (Nos. 65 and 66) in this group died twenty-three and twenty-one days after infection, respectively. The local lesions of both were small and slightly necrotic. The regionary inguinal lymph nodes, too, were small. The spleens were small, and in the case of the animal which died twenty-three days after infection two minute tubercles showed grossly in the spleen. There was no macroscopic evidence of generalized tuberculosis in either animal.

COMMENT

All but two of the treated animals (Nos. 59 and 60) of this series appeared to be benefited by sulfanilamide.

SERIES 7

Twenty-two guinea pigs weighing, on the average, 340 Gm. were infected subcutaneously with 1 c.c. of the suspension. Eleven were kept as controls; six were first treated three days after infection, and five, ten days after infection. Four of the six guinea pigs first treated three days after infection received 480 mg. (105, 105, 105, 165) of sulfanilamide daily on the 4th, 5th, 7th, 8th, 11th, 12th, 14th, 15th, 18th, 19th, 21st, 22nd, 25th, and 26th days after infection. Because some of the treated animals were either losing slightly in weight or barely maintaining their weight, the daily dose of the drug was reduced to 420 mg. (105×4) daily, given on the 29th, 30th, 33rd, and 34th days after infection. Two treated animals in the above group died before the completion of the experiment. One (No. 78) died thirteen days after infection, and the other (No. 77), seventeen days after infection. In both, the regionary inguinal lymph nodes were barely palpable, and the local lesions could not be detected. There was no gross evidence of tuberculosis in any of the organs.

Three of the five animals first treated ten days after infection received 540 mg. (105, 165, 105, 165) of sulfanilamide as a total daily dose on the 11th, 12th, 14th, and 15th days after infection. Because of loss in weight, the daily dose of the drug was reduced to 480 mg. (105, 105, 105, 165) which was given on the 18th, 19th, 21st, 22nd, 25th, 26th, 29th, 30th, 33rd, and 34th days after infection. Treated animal No. 82 died twenty days after infection, and No. 83 died fifteen days after infection. The regionary inguinal lymph nodes of both these animals were only slightly enlarged. The local lesion of the animal (No. 82) which died twenty days after infection was small, but slightly necrotic. Three control animals died during the course of the experiment: One (No. 93), died thirteen days after infection; another (No. 94) died sixteen days after infection. Both showed slightly enlarged regionary inguinal lymph nodes. The third control animal (No. 91) died twenty-nine days after infection. The local lesion of this animal was necrotic, and the regionary inguinal lymph nodes were greatly enlarged. There was moderate generalized tuberculosis in this instance. Control animal No. 92, which was sacrificed thirty-three days after infection, showed a very extensive local lesion and extensive generalized tuberculosis. Treated animal No. 76 of this series failed to maintain its weight during the course of treatment.

TABLE III

	NO.	WEIGHT		NO. DAYS TREATED	AVERAGE TREATMENT DOSE (MG.)	TOTAL DOSE (MG.)	AVERAGE DAILY DOSE (MG.)	DEGREE MACROSCOPIC TUBERCULOSIS			SIZE OF				D.	S.
		B.I.	P.M.					SPLEEN	LIVER	LUNGS	L.L. (MM.)	R.N. (MM.)	T.B.N. (MM.)	SPLEEN (MM.)		
Series 6 (Average Weight, 310 Gm.)																
Treated 3 days after infection	55	320	405	18	420	7,560	236	±	–	–	21×17	7×6	13×4	22×12		35
	56	320	375	18	420	7,560	236	+	–	±	12×9	5×3	9×3	28×14		35
	57	315	300	18	420	7,560	236	+	–	+	21×14	3×2	8×5	26×12		35
	58	305	325	18	420	7,560	236	+	–	+	22×18	3×2	6×4	25×13		35
	59	300	280	14	420	5,880	184	++	+	+	24×21	11×6	9×4	30×15		35
	60	300	255	14	420	5,880	184	+	++	++	13×9	6×2	4×3	34×16		35
Treated 10 days after infection	61	315	415	14	445	6,240	250	+	+	+	19×18	9×5	6×3	37×15		35
	62	310	380	14	445	6,240	250	+	–	±	24×21	12×9	6×5	25×11		35
	63	310	385	14	445	6,240	250	±	–	±	18×15	8×7	6×3	27×13		35
	64	305	370	14	445	6,240	250	+	–	±	21×13	11×7	8×5	31×11		35
Controls	67	300	450					+	+	++	24×19	13×9	12×10	30×15		35
	68	320	325					++	+	+	35×20	14×12	12×5	41×18		35
	69	310	440					++	–	++	26×19	12×8	12×7	31×15		35
	70	310	390					++++	+	+	19×17	14×10	14×12	36×21		35
	71	315	385					+	–	+	25×18	15×9	11×5	25×11		35
	72	305	405					+++	+	+	23×18	11×7	8×4	38×18		35
Series 7 (Average Weight, 340 Gm.)																
Treated 3 days after infection	73	340	325	18	466	8,400	266	+	+	+	21×16	5×3	8×5	28×11		35
	74	330	370	18	466	8,400	266	±	–	–	23×18	7×4	9×6	26×12		35
	75	325	380	18	466	8,400	266	±	+	+	18×12	9×5	6×3	29×13		35
	76	355	310	18	466	8,400	266	++	+	+	20×14	12×4	8×6	30×14		35
Treated 10 days after infection	79	340	355	14	497	6,960	278	+	–	–	25×15	11×6	9×5	30×12		35
	80	360	360	14	497	6,960	278	+	+	+	12dia.	14×7	10×5	31×15		35
	81	330	375	14	497	6,960	278	+	–	–	21×20	9×7	8×6	28×12		35
Controls	84	325	440					+++	+	++	29×20	14×10	14×9	37×18		35
	85	335	450					+++	+	+	26×23	10×8	22×18	42×22		35
	86	340	425					++	+	++	23×20	15×11	9×6	28×12		35
	87	355	385					+++	++	++	29×21	14×8	14×9	39×17		35
	88	335	425					++++	–	++	28×19	14×9	16×9	40×21		35
	89	360	610					++++	++	+	34×25	16×12	14×8	41×18		35
	90	350	475					++++	+	+	27×22	12×10	12×8	34×16		35
	91	360	330					++	–	+	22dia.	14×7	17×12	36×18	29	
	92	325	310					++++	++	++	32×18	15×9	17×6	40×24		33

L.L. = local lesion.
R.N. = largest regionary node.
T.B.N. = largest tracheobronchial node.
dia. = diameter.
For explanation of other abbreviations and symbols, see footnotes to Table I.

COMMENT

All treated animals referred to in Table III appeared to be benefited by sulfanilamide. (Fig. 2 and Table III.)

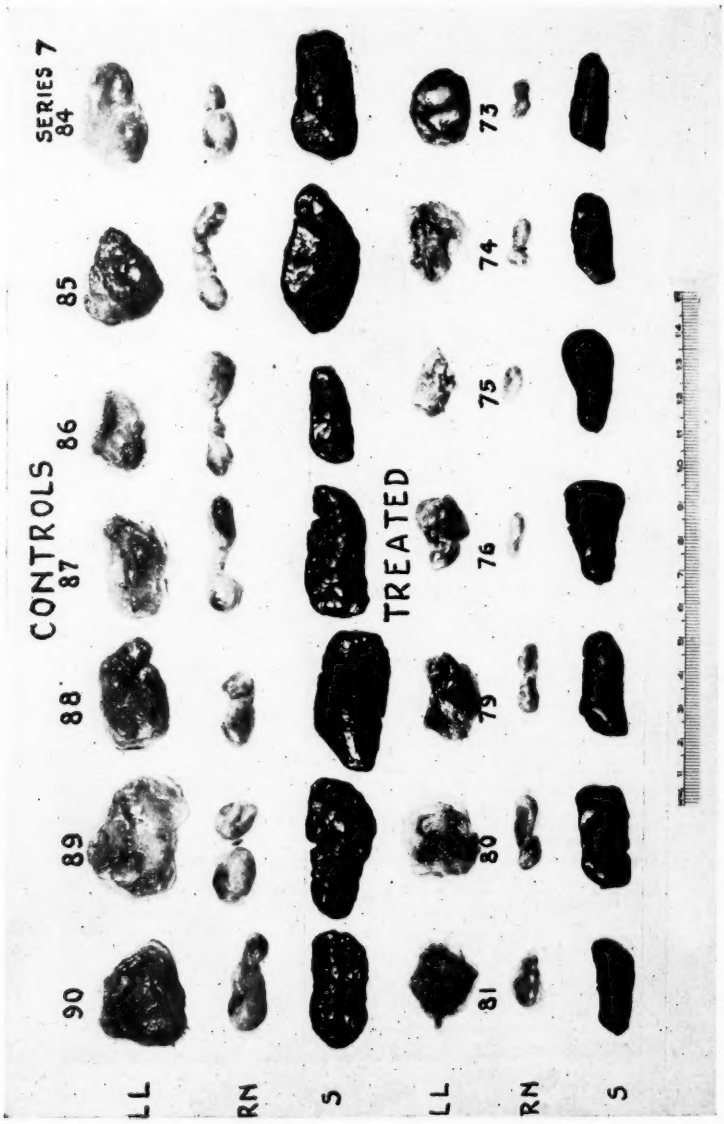

Fig. 2.—Series 7. *S*, Spleen; *RN*, regionary inguinal lymph node; *LL*, local lesion. Consult the text and Table III for further details.

SERIES 8

Seventeen guinea pigs weighing, on the average, 385 Gm. were infected with 1 c.c. of the suspension. Eight were kept as controls, five were treated three days after infection, and four were treated ten days after infection.

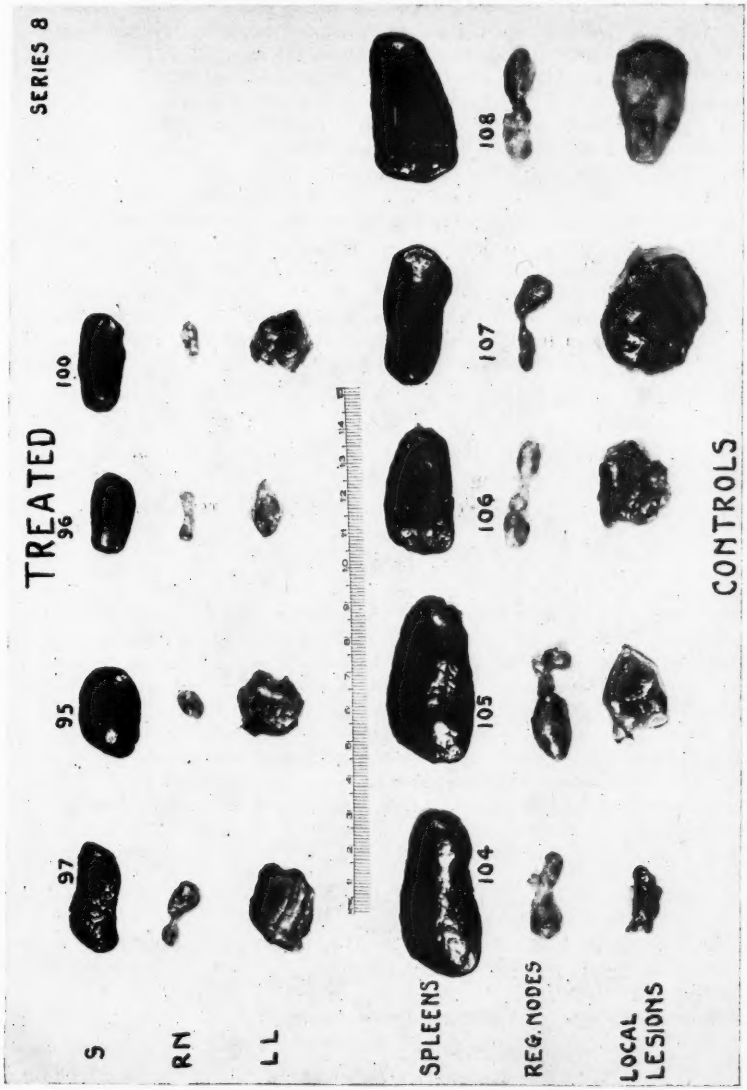

Fig. 3.—Series 8. Note the differences between the sizes of the spleens and regionary inguinal lymph nodes of treated and control animals. Consult the text and Table IV for details of the experiment.

Three of the five animals first treated three days after infection received 540 mg. (105, 165, 105, 165) of sulfanilamide on the 4th, 5th, 7th, 8th, 11th, 12th, 14th,

15th, 18th, 19th, 21st, and 22nd days after infection. The daily dose of sulfanilamide was then reduced to 480 mg. (105, 105, 105, 165) given on the 25th, 26th, 29th, 30th, 33rd, and 34th days after infection. Animal 99 in this group, which showed a slightly enlarged regionary node, died fourteen days after infection. Animal 98, treated similarly to those referred to above, was sacrificed thirty-three days after infection. This animal, in addition to findings which have been tabulated, showed a small regionary node and a large local lesion. One (No. 103) of the four animals treated ten days after infection died fourteen days after infection. It had received only two treatments of 600 mg. (105, 165, 165, 165) of sulfanilamide on the eleventh and twelfth days. The regionary node of this animal was slightly enlarged. Two animals (101 and 102) were sacrificed thirty-three days after infection. Both had received 6,480 mg. of sulfanilamide given on twelve treatment days as follows: 600 mg. (105, 165, 165, 165) on the 11th, 12th, 14th, and 15th days after infection; 540 mg. (105, 165, 105, 165) on the 18th, 19th, 21st, and 22nd days; 480 mg. (105, 105, 105, 165) on the 25th, 26th, 29th, and 30th days after infection. Animal No. 100, which was sacrificed thirty-five days after infection, received two additional treatments on the thirty-third and thirty-fourth days after infection. Two control animals (Nos. 109 and 110), which were sacrificed on the thirty-third day after infection, had very large regionary lymph nodes and large, ulcerated, local lesions. Both showed enlarged spleens and numerous tubercles in the spleen, liver, and lungs. Control animal No. 111, which died fourteen days after infection, showed a slightly enlarged inguinal node.

COMMENT

In no other instance in all our experiments did what might be called an adequately treated animal do as poorly as No. 97. All other treated animals in this series appeared to benefit from the treatment. (Fig. 3.)

SERIES 9

Twelve guinea pigs weighing, on the average, 460 Gm. were infected subcutaneously with 1 c.c. of the suspension. Six were treated; six were kept as controls. Treatment with 660 mg. (165×4) of sulfanilamide was started on the eleventh day after infection. Similar daily doses of the drug were given on the 12th, 14th, and 15th days after infection. The daily dose of the drug then decreased to 600 mg. (105, 165, 165, 165) and was given on the 18th, 19th, 21st, 22nd, 25th, 26th, 29th, 30th, 33rd, and 34th days after infection. Three animals died during the course of the treatment; one (No. 117) died seventeen days after infection; another (No. 116) died twenty days after infection; and the third (No. 115) died twenty-one days after infection. All three were free of gross tuberculous lesions. Control animal No. 123 died twenty-three days after infection. The local lesion in this instance was moderately necrotic, and the regionary node was definitely enlarged.

COMMENT

All animals in this series referred to in the table appeared to be benefited by the treatment. (Table IV.)

HISTOLOGIC EXAMINATION

The lungs, livers, spleens, kidneys, and the locally infected sites and draining lymph nodes of treated and control animals referred to in Experiments 1 to 9, inclusive, were examined microscopically. This examination was completely objective. New numbers were given to all animals; the renumbered histologic preparations were then examined histologically. As nearly as possible, complete

TABLE IV

	NO.	WEIGHT		NO. DAYS TREATED	AVERAGE TREATMENT DOSE (MG.)	TOTAL DOSE (MG.)	AVERAGE DAILY DOSE (MG.)	DEGREE MACROSCOPIC TUBERCULOSIS			SIZE OF				D.	S.
		B.I.	P.M.					SPLEEN	LIVER	LUNGS	L.L. (MM.)	R.N. (MM.)	T.B.N. (MM.)	SPLEEN (MM.)		
Series 8 (Average Weight, 385 Gm.)																
Treated 3 days after infection	95	395	400	18	520	9,360	293	+	+	−	19×17	9×6	12×4	27×13		35
	96	365	410	18	520	9,360	293	±	−	−	16×10	4×3	11×6	24×13		35
	97	390	355	18	520	9,360	293	+++	++	++	25×20	11×7	11×6	33×14		35
	98	385	260	16	525	8,400	280	+	−	−	30×12	5×3	6×4	25×12		33
Treated 10 days after infection	100	400	395	14	530	7,440	300	±	+	+	16dia.	11×4	10×4	30×13		35
	101	395	300	12	540	6,480	282	+	−	−	10×8	10×6	10×5	28×14		33
	102	385	245	12	540	6,480	282	+	++	−	12dia.	7×4	10×4	22×11		33
Controls	104	370	420					++++	++++	+++	17×6	11×7	16×8	50×22		35
	105	385	405					++++	+	++	22×17	20×10	14×7	48×26		35
	106	395	440					+++	+	++	22×21	15×6	13×8	37×21		35
	107	390	375					+	++++	+++	36×27	12×6	12×9	41×17		35
	108	365	445					+++	+	++	34×25	16×8	13×7	45×24		35
	109	375	370					+++	+	+	27×19	18×8	15×8	38×20		33
	110	390	525					++	+	++	24×16	17×11	16×7	36×17		33
Series 9 (Average Weight, 460 Gm.)																
Treated 10 days after infection	112	445	505	14	617	8,640	346	-	−	+	14×8	7×5	10×7	30×14		35
	113	460	450	14	617	8,640	346	+	−	−	12×10	7dia.	10×6	28×14		35
	114	485	425	14	617	8,640	346	++	+	−	20dia.	12×6	12×8	35×17		35
Controls	118	480	510					+++	+	+	20×18	21×10	15×12	40×19		35
	119	485	505					++	−	++	21×16	12×7	15×6	40×17		35
	120	450	525					+++	−	++	23×17	13×9	18×11	33×15		35
	121	475	500					++++	+	+	22×18	11×9	23×11	38×18		35
	122	445	585					++++	−	+++	27×19	11×7	8×5	55×23		35

For explanation of the abbreviations and symbols, see footnotes to Tables I and III.

sagittal sections of spleen, kidney, and liver were taken; all sections of lung consisted of the entire right lower lobe.

Sites of Infection and Draining Lymph Nodes.—No appreciable microscopic difference could be detected between the types of infection noted in the local lesions of treated and control animals. Tuberculous tissue, together with nonspecific granulation tissue, was present in all instances. The extent of surface ulceration appeared to be more dependent upon secondary infection than upon the effects of treatment. Although the lymph nodes in all cases were extensively involved by the tuberculous process, the nodes were, in general, appreciably smaller in the treated animals as compared with those of the control animals.

Spleen.—Microscopically, this organ was found to be involved in almost every instance in both treated and control animals. When the degree of tuberculosis in treated animals was moderate, the spleens were found to exhibit a greater tendency to endothelioid proliferation and showed less necrosis than did the spleens of control animals. When, however, the spleens of treated animals were found to be extensively involved, then it became impossible to recognize any appreciable differences between the degree of necrosis found in spleens of treated and control animals. The most striking difference between treated and control animals appeared to be in the size of the spleen. In practically every instance the spleen of the control was appreciably larger than the spleen of the treated animal. In a number of the treated animals a considerable amount of phagocytosed, iron-bearing pigment was found within endothelioid cells. The significance of this finding is not known. From a correlation between the gross and microscopic findings, it is suggested that perhaps the best criterion available, at present, for estimating the retarding or inhibitory effect that sulfanilamide appears to exert is to be found in the size and appearance of the spleen of the treated animals when compared with that of the control.

Liver.—Microscopically, the involvement of the liver in both control and treated animals paralleled the degree of involvement of the spleen. In those cases in which only slight tuberculosis of the spleen was present, the liver showed only minimal, rare, isolated lesions, or no lesions at all. Where the tuberculosis of the spleen was massive, the liver also showed extensive tuberculosis in most instances, but in every case the degree of involvement was less than that observed in the spleen. In no case was the amount of tuberculosis greater in the liver than in the spleen of the same animal, whether treated or control. The amount of necrosis in the tuberculous lesions in the liver paralleled that seen in the spleen.

Lung.—The presence and extent of tuberculous involvement of the lungs was inconstant. No striking differences could be distinguished between the histologic pictures found in the lungs of treated and control animals. In the majority of animals the amount of involvement of the lungs paralleled that seen in the liver and spleen. In a considerable number of animals, however, this was not the case. The lesions in the lungs showed typical tubercles with only minimal necrosis and small foci of tuberculous pneumonia. Since there was, in general, a greater degree of tuberculosis in the untreated animals, it may be said that the incidence and degree of lung involvement were greater in the control than in the treated animals.

Kidney.—In only five animals in the entire series was microscopic evidence of tuberculosis present in the kidneys. This was minimal in amount, and no necrosis was present in any of the tubercles. The occurrence of the lesions in the kidneys did not parallel that found in any other organs, for tuberculous lesions of the kidney were found in animals with only moderate spleen and liver involvement without lung tuberculosis, and in animals with extensive disease. The lesions were found in both treated and control animals.

COMMENT

The objective, quantitative, microscopic grading of the amount of tuberculosis closely approximates the macroscopic grading in all animals of this series. In general, the draining lymph nodes and the spleens were smaller, and there was less necrosis in the spleens of treated animals than in those of controls. The amount of tuberculosis in the other organs roughly parallels that found in the spleens of the same animals, with the exception of the kidneys, which appear to be relatively infrequently involved.

DISCUSSION OF EXPERIMENTS 1 TO 9, INCLUSIVE

Series 1 to 9 represent 123 guinea pigs of varying weights infected with virulent human tubercle bacilli. Seventy-one were treated; fifty-one were kept as controls.

Treated Three Days After Infection.—Seventeen guinea pigs were treated three days after infection. Of these, fourteen survived for a period satisfactory for the experiment. Three (Nos. 77, 78, and 79) of these treated animals died during the course of the experiment. One (No. 98) was sacrificed thirty-three days after infection. Ten treated guinea pigs in this series were sacrificed at the conclusion of the experiment, namely, thirty-five days after infection. Animals 59, 60, and 97 were not benefited by treatments. Eleven of the fourteen guinea pigs treated three days after infection and referred to above appeared to be benefited by the treatments with sulfanilamide.

Treated Ten Days After Infection.—Forty-nine guinea pigs were treated ten days after infection. Of these, thirty-two survived for a period satisfactory for the experiment. Nineteen of the thirty-two were in the experiments carried on for fifty days. Sixteen of these treated animals were sacrificed at the conclusion of the experiment. Animal 28 died forty days after infection; No. 40 died forty-five days after infection, and No. 48 died on the fiftieth day after infection. All but four (Nos. 26, 27, 38, and 40) of the nineteen animals referred to above appeared to be benefited by the sulfanilamide treatments. Thirteen animals first treated ten days after infection are under discussion in the experiments which were terminated thirty-five days after infection. Animals 101 and 102 were sacrificed thirty-three days after infection. The remaining eleven treated animals were sacrificed at the conclusion of the experiment. All thirteen treated guinea pigs in the series under discussion appeared to be benefited by the sulfanilamide treatments. Twenty-eight of the thirty-two guinea pigs first treated ten days after infection and which have been referred to in the tables and text have been considered as benefited by the treatment which they received.

Treated Sixteen Days After Infection.—Five animals were treated sixteen days after infection. Four survived for a period satisfactory for the experiment. The number of treated animals is too few to permit of any additional comment.

TABLE V

	NO.	WEIGHT		NO. DAYS TREATED	AVERAGE TREATMENT DOSE (MG.)	TOTAL DOSE (MG.)	AVERAGE DAILY DOSE (MG.)	DEGREE MACROSCOPIC TUBERCULOSIS			SIZE OF				D.	S.
		B.I.	P.M.					SPLEEN	LIVER	LUNGS	L.L. (MM.)	R.N. (MM.)	T.B.N. (MM.)	SPLEEN (MM.)		
Series 10 (Average Weight, 420 Gm.)																
Treated 3 days after infection	1	405	415	14	591	8,280	244	+	–	–	32×14	4×3	11×5	28×13		35
	2	410	385	14	591	8,280	244	–	–	–	16×8	4×3	8×4	27×10		37
	3	420	445	14	591	8,280	244	–	–	–	25×20	5×3	10×5	29×15		37
Treated 10 days after infection	5	410	490	10	624	6,240	231	–	–	–	24×20	7×4	9×6	28×11		37
	6	425	530	10	624	6,240	231	–	–	–	24×22	4×3	11×6	27×14		37
	7	440	490	10	624	6,240	231	+	–	+	7×5	4×3	11×6	33×15		37
Controls	9	435	560					+ +	–	–	14×11	4×3	9×4	28×18		35
	10	420	560					+	–	–	30×19	12×8	17×10	33×17		37
	11	430	505					+	+	+	29×28	14×7	13×7	35×17		37
	12	415	510					–	+	+ +	30×28	7×3	19×12	31×14		37
	13	425	555					–	+	+	26×21	8×4	11×7	30×14		37
	14	440	560					+	+	+	30dia.	17×10	11×10	35×17		37
	16	420	545					+	–	–	27×18	16×8	18×9	34×15		32

For explanation of abbreviations and symbols, see footnotes to Tables I and III.

Controls.—Six of the fifty-one controls died before the conclusion of the experiment. Twenty-four of the seventy-two treated animals died before the experiments were terminated.

SERIES 10: BOVINE

Sixteen guinea pigs weighing, on the average, 420 Gm. were infected subcutaneously in the groin with 1 c.c. of a suspension of *bovine tubercle bacilli* (B_1 Saranac Lake). A smear of this suspension showed one bacillus per 100 power oil immersion field. Eight guinea pigs were kept as controls; four were treated three days after infection, and four, ten days after infection. The four animals first treated three days after infection were given 600 mg. (105, 165×3) of sulfanilamide on the 4th, 5th, 7th, 8th, 11th, 12th, 14th, 15th, 18th, 19th, 21st, and 22nd days after infection. The total daily dose of sulfanilamide was then reduced to 540 mg. (105, 165, 105, 165) given on the 25th and 26th days after infection. One of the treated animals (No. 4) died nineteen days after infection. This animal was free of gross tuberculosis.

The four animals first treated after ten days of infection received 660 mg. of sulfanilamide (165×4) on the 11th, 12th, 14th, and 15th days after infection. The dose was then decreased to 600 mg. (105, 165×3) daily, given on the 18th, 19th, 21st, 22nd, 25th, and 26th days after infection. One treated animal (No. 8) which died twenty-two days after infection was free of gross tuberculosis, save for one tubercle in the spleen. Control animal No. 15 died eighteen days after infection. It was free of infection. Control animal No. 16 was sacrificed thirty-two days after infection. All treated and control animals which survived were sacrificed thirty-seven days after infection. The important findings of animals which survived for a period satisfactory for the experiment have been tabulated.

COMMENT

Under the conditions of our experiment, sulfanilamide appeared to exert a slight inhibitory effect upon the development of experimental bovine tuberculosis in the guinea pig. (Table V.)

SUMMARY

The recorded results of our Experiments 1 to 9, inclusive, again demonstrate the inhibitory effect of sulfanilamide upon the development of experimental tuberculosis in the guinea pig. In by far the majority of instances, the local lesions of treated animals were smaller and, in most instances, were grossly less necrotic than those of controls. The regionary inguinal nodes, tracheobronchial nodes, and spleens of treated animals as well were smaller. In addition, the spleen, liver, and lungs of treated animals, in the majority of instances, showed much less macroscopic tuberculosis than did similar organs of the control animals. This inhibitory effect was obtained even though treatment was interrupted at intervals. We had previously drawn attention to this possibility.

We are of the opinion that, under the conditions of our experiments, it is permissible to conclude that the dose of sulfanilamide on treatment days should be from 1.38 to 1.45 Gm. per kilogram of weight. The maximum tolerated and what would be regarded as an adequate daily dose for the entire treatment period was found to be from 0.70

to 0.75 Gm. per kilogram of body weight. This statement does not mean to imply that, were such a dose given daily, the inhibitory effect would be as striking as is the case when larger doses of the drug are given on indicated treatment days and no drug given on rest days.

It would perhaps be preferable to start with smaller treatment doses during the first five days of the experiment. Animals first treated ten days after infection should receive treatments on twenty days during the course of a fifty-day experiment, and on fourteen days during the course of a similarly conducted thirty-five-day experiment. We regard the oral route for the administration of the drug as satisfactory. Animals first treated ten days after infection responded just as satisfactorily to sulfanilamide as did animals first treated three days after infection. Animals first treated sixteen days after infection did not respond to treatment. The number of animals so treated is thus far too few to permit of further comment. In this connection it should be noted that Greey, Campbell, and Culley were unable to note any macroscopic differences between treated and control animals when treatment was started seventeen and twenty-four days after infection.

All of our animals were infected subcutaneously in the groin. The infective doses which we employed will produce extensive tuberculosis in the guinea pig within six weeks. This infective dose is less than that used by Rich and Follis and by Greey and his co-workers. Buttle and Parish and Kolmer and his associates gave massive infective doses. Contrary to Greey, Campbell, and Culley, we did not find albino guinea pigs inferior to other breeds. Our animals received a well-balanced diet; the water intake was controlled.

An important consideration with regard to the tolerance of the drug is the body weight of the individually treated animal at all stages during the course of the experiment. Many of the control animals gained in weight. This fact in no way detracts from the observation that a treated animal which maintains its weight, or better still, gains in weight, will benefit more from the administration of sulfanilamide than a treated animal which loses in weight. The weights of our guinea pigs were recorded previous to the beginning of a treatment day. In many instances, as already indicated, the amount of sulfanilamide given to a particular animal was influenced by the weight curve. A loss in body weight of 5 per cent or less was not regarded as significant. When the weight loss exceeded 5 per cent, the rest period was prolonged. Most guinea pigs which lost 10 per cent of their body weight during the course of the experiment did poorly, and, in many instances, failed to survive the experiment. Control animals fed blank capsules during treatment periods showed more extensive lesions and a lesser gain in weight than unhandled controls.

We are of the opinion that, when the total daily dose of sulfanilamide is given in divided doses, a more constant level of sulfanilamide in the body is maintained. The possibility of toxic manifestations is thereby lessened. Under the conditions of our experiments, the level of sulfanilamide in the blood after a two-day rest period was found to be at times about 2.5 mg. per 100 c.c. Some of our animals which died from too much sulfanilamide had blood levels of 75 mg. (30 mg. of free and 45 mg. of acetylated) sulfanilamide. We again draw attention to the fact that the spleens of treated animals were darker than those of the control animals.

In examining the tabulated findings of our experiments, cognizance should be taken of the fact that *some of the treated animals did not receive as much sulfanilamide as they should have received according to their body weight.* We are of the opinion that some of the poor results reported by others are due, in part at least, to inadequate dosage.

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THE PEDICLED MUSCLE FLAP IN THE TREATMENT OF BRONCHIAL FISTULAS

Report of 16 Cases

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As early as 1900 Abrashanoff published in a Russian periodical the report of a case of bronchial fistula which he treated with a pedicled muscle flap. Since then he has written two papers, the last in 1911, describing four more cases treated with muscle flaps, two of which were bronchial fistulas, one a vesicovaginal fistula, and one a rectovaginal fistula. Abrashanoff is undoubtedly the pioneer in this field.

During the next decade a number of authors occupied themselves with this subject. Foremost among them are Eggers, Lebosche, Carter, Nissen, Pool, Garlock, Ritter, Scrimger, Steinbruch, Wangensteen, and Lezius.

A detailed bibliography is given by Wangensteen and Carter.

In Sweden, Key has advocated this method and reported two cases at the Scandinavian Congress of Surgeons held in 1933. In the same year, at a meeting of the Tuberculosis Medical Association, he reported one case of tuberculous bronchial fistula closed with a pedicled muscle flap, and in 1934 and 1935 he described four more cases at the Swedish Surgical Association.

Since 1935, sixteen operations of this type have been performed on thirteen patients at Surgical Clinic II of Sabbatsberg Hospital. Of the three cases in which the operation was performed twice, one was a failure and had to be reoperated, and the other two were bilateral. In all the cases it was a question of residual cavities after pulmonary abscesses due, in one case, to a congenital cyst, in two cases to pulmonary embolism combined with septic liquefaction, in one case to inhalation of the contents of the stomach under narcosis, and in the rest to postpneumonic complications. Bronchial fistulas were present in all the cases.

The time elapsing between the opening of the abscess and the plastic operation has varied between one and one-half and twenty months. In eleven cases the muscle implant was made within three and one-half months. In three cases, more than five months elapsed because of reasons not connected with the cavity itself. In one case a duodenal fistula had been closed; in another a new abscess on the other

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side had been treated, and in the third the time had been taken up partly in excision of the congenital cyst and partly in an attempt to have the remaining fistula close in some other way.

One of the plastic operations was performed in 1935, two in 1936, four in 1937, and nine in 1938.

The technique was as follows:

When the abscess was opened great care was taken to provide for wide drainage, which was done by resecting one or more ribs and removing the corresponding portions of the intercostal muscles, pleura, and outer wall of the lung cavity by means of diathermy. The intercostal nerves were isolated and divided, and the central stump was injected with alcohol to prevent the radiating pains which sometimes remain for a long time after the operation. Tamponage of the cavity was done, and great care was taken when changing the dressings to keep the opening as wide as possible so that the infection should heal as quickly as possible. It has occasionally been sufficient to insert the flap through the opening in the chest wall into the cavity, if the latter was relatively small. However, when the cavities were more extensive and particularly when they seemed large in comparison with the orifice, the opening was enlarged, either by making a larger hole in the soft parts or by resecting one or two more ribs. Great care has been taken to make the flap long enough and wide enough to fill the cavity completely in order not to leave any space in which secretion could stagnate. In this connection it must be borne in mind that, after excision, the flap tends to contract rather greatly. It is essential that it be well nourished right out to its tip. Whenever possible it has been attempted to keep the innervation undisturbed in order to save the flap from atrophy. Furthermore, it has been made a point to have the base of the flap broad immediately next to the orifice and to avoid using muscles with too much tendinous tissue, as, for example, the sacrospinalis. The latissimus dorsi and pectoralis major have, therefore, been preferred. However, in one case in which the operation had to be redone, the long dorsal muscles were used. No reason has been seen to adopt Garlock's suggestion and place a special little slip of the graft in the bronchial fistula itself, like a cork in a bottle.

One of the earlier cases showed an extensive subcutaneous emphysema reaching all the way from the groin to the axilla. In order to avoid such complications, fine catgut sutures have been made between the flap and the edge of the cavity by way of reinforcement. However, a slight transitory emphysema has been found despite this precaution. In one case the operation had to be repeated due to the flap's becoming necrotic because of infection and development of a cavity filled with stagnant secretion, which necessitated renewed drainage. This might possibly have been avoided had the cavity been entirely filled with the implant.

One of the patients developed a hematoma with infection and a subcutaneous emphysema, as well as a temporary communication to the bronchus which, however, closed spontaneously within three or four weeks and was entirely healed within five weeks. In some of the cases the wounds were drained with a small tube, while in others the wound was sutured primarily. However, it was occasionally necessary to puncture a hematoma or to institute secondary drainage. All the

cases, with one exception, healed within a relatively short time. The interference had no effect to speak of upon the patients, and no deaths occurred.

All the patients have undergone postoperative examination with regard to their working capacity, dyspnea, the amount of sputum, healing, subjective troubles, etc. Roentgenograms were also made. Only one operation failed, inasmuch as necrosis and infection intervened and spoiled the results, which in all the other cases were good. In two cases, however, asthma, the original complaint, caused permanent trouble, which, of course, had nothing to do with the operation. The defect remains in the muscle from which the flap was taken, but in no case does it appear to have had any ill effects. In cases in which more than one rib was removed, there sometimes remains a pulmonary hernia which bulges upon coughing, but otherwise causes no trouble.

One advantage of this method is that it often shortens the period of healing considerably. The time elapsing between this operation and the patient's discharge has varied between twelve days and six weeks. As a result, we now make it a practice to close residual cavities with bronchial fistulas as soon as the infection in the cavities permits. We have not waited until cultures from the cavity gave negative results, since this would probably have meant an interminable delay, but only until the cavity appeared to be clean and free from irritation, and smears did not show any great bacterial growth. However, the appearance of streptococci has constituted a contraindication. Nor has time been wasted in waiting for the fistula to heal spontaneously.

It is uncertain what happens to the flap after the operation. Lezius is of the opinion that, under the influence of the infection always to be found in the residual cavity, it becomes transformed into fibrous tissue and forms a massive scar shutting off the bronchus exteriorly. An attempt to solve this problem has been made by Pool and Garlock, who made bronchial fistulas in dogs and then plugged them with pedicled muscle flaps. A year later the dogs were killed, and the authors were able to show that the muscle tissue was still alive and that the bronchial epithelium directly covered the muscle surface, no transformation into fibrous tissue having taken place.

To summarize, it may be stated that plastic operation with a pedicled muscle flap has shown itself to be an excellent therapeutic method in residual cavities with bronchial fistulas. It can be performed relatively soon after the abscess has been opened and shortens the healing period to a considerable extent. It is particularly indicated in cases of small and medium-sized cavities and *Gitterlungen*, but is less advisable in big cavities which cannot be made to decrease in size with conservative treatment. Possibly the latter cases could be treated by a method which we have not yet used, namely, packing the cavity with fat. This treatment is but little strain on the patient and, in the majority of cases, gives good results within a short time. The subsequent course is also good.

CASE REPORTS

CASE 1.—Female, 36 years old, with an appendicular abscess, a pulmonary embolism, and a pulmonary abscess. Drainage was instituted by resecting 9 cm. of the tenth rib on the right side. Eight months later there was a residual cavity the size of a walnut with a bronchial fistula which was closed with a pedicled muscle flap from the latissimus dorsi, the bronchial stump having first been dissected free to a depth of 1 cm. and tied off, after which the lung tissue was excised in a wedge and sutured. The long wait of eight months had been devoted to drainage of a subphrenic abscess and closure of a duodenal fistula. The wound healed in five weeks. Follow-up examination two and one-half years later revealed the condition to be good.

CASE 2.—Male, 50 years old, with asthma, bronchitis, bronchopneumonia, and pulmonary abscess. Drainage was instituted by resecting 10 cm. of both the ninth and tenth ribs on the left side anteriorly from the angulus costae. Three months later a pedicled muscle flap from the latissimus dorsi was implanted in a superficial cavity the size of half an egg with two bronchial fistulas. The case was complicated by a large subcutaneous emphysema, extending from the groin up toward the neck. The emphysema receded in a week, and the wound healed in six weeks. Follow-up examination two and one-half years later revealed bronchial asthma as before and bulging in the scar upon coughing. Otherwise, the condition was good.

CASES 3 and 8.—Female, 43 years old, with nephrolithiasis. Operation was performed. There was a pulmonary abscess which later was found to be an infected congenital cyst. Thoracoplasty was done, but the cavity still remained, although reduced in size. Drainage was instituted by resecting regenerated ribs and the superficial pulmonary layer outside the cyst. Healing did not take place. The cyst was excised. The wound healed with bronchial fistulas. Cauterization was done in an attempt to make the fistulas close, but without result. Ten months later a pedicled muscle flap from the latissimus dorsi was implanted in a shallow cavity half the size of a fist with two bronchial fistulas. The wound healed well, but the amount of sputum gradually increased and a cavity containing stagnant secretion developed. The cavity had to be drained after waiting fifteen months for spontaneous healing. Four months later another muscle implant from the sacrospinalis was successfully made in a cavity half the size of a banana with bronchial fistulas. The wound healed in a little more than three weeks. Follow-up examination one year after the last operation showed the wound to be healed. There were occasional small amounts of sputum, but the patient was otherwise in good condition.

CASE 4.—Male, 23 years old, with bronchial asthma, bronchopneumonia, and pulmonary abscess. Drainage was instituted by resecting 10 cm. of the sixth, seventh, and eighth ribs next to the spinal column. A cavity the size of a fist was found. After six weeks there remained a cavity the size of a tangerine with one large and two small bronchial fistulas, for which reason a pedicled muscle flap from the latissimus dorsi was implanted. The wound healed in three weeks. Follow-up examination one and one-half years later showed the healing to be good. The patient had no cough and was in good general condition.

CASE 5.—Female, 27 years old, with pneumonia and pulmonary abscess. Drainage was instituted by resecting the tenth rib in the scapular line. A large cavity remained in toward the hilus and drained poorly. Two months after the first operation, 10 cm. were resected from the fifth to the ninth rib. Six weeks later there remained a cavity the width of a banana with bronchial fistulas which extended up toward the hilus pulmonis. A pedicled muscle flap from the latissimus dorsi was implanted. The wound healed in three weeks. Follow-up examination one and one-half years later showed the wound to be healed and the results to be good.

CASE 6.—Female, 27 years old, with chronic bronchitis, bronchopneumonia, and pulmonary abscess. Drainage was instituted by resecting the third rib anteriorly on the right side. Three months later a pedicled muscle flap from the pectoralis major was implanted in a cavity nearly as big as an orange with bronchial fistulas. The wound healed in two and one-half weeks. Follow-up examination one year and three months later showed the patient to be in good condition and able to work. There was some bulging in the rib defect on the anterior aspect when the patient coughed, and there was a defect in the inferior part of the pectoralis muscle, which, however, caused no trouble.

CASE 7.—Female, 33 years old, with pneumonia and pulmonary abscess. Drainage was instituted by resecting the third rib anteriorly on the right side. Two months later a pedicled muscle flap from the pectoralis major was implanted in a cavity with bronchial fistulas, which, when a further segment of the third rib was resected, was found to be as wide as a banana and a few centimeters deep. The wound healed in two weeks. Follow-up examination ten months later showed the patient to be in good condition and able to work. There was a defect in the pectoralis muscle which caused no trouble.

CASES 9 and 10.—Male, 43 years old, with pneumonia and pulmonary abscess which had been lying paramediastinally on the right side for nine months. Operation was done for drainage. There were no pleural adhesions. Eight centimeters of the fifth to the eighth rib were resected anteriorly from the vertebral column, and paraffin plombage was done. Three weeks later drainage of an abscess found at a depth of 10 cm. was instituted. Two months later another abscess found on the left side was unsuccessfully treated with bronchoscopy. Six and one-half months after the last operation 10 cm. of each the third and fourth ribs was resected in the axilla on the left side. There were no pleural adhesions. Plombage was done. Four weeks later drainage was instituted of an abscess at a depth of 4 cm. After a further period of six weeks a pedicled muscle flap from the latissimus dorsi was implanted in a walnut-sized cavity on the right side with fistulas. The wound healed in three weeks. Six weeks after the first plastic operation another one was done with a pedicled flap from the latissimus dorsi in a walnut-sized cavity with a fistula. The wound healed in three and one-half weeks. Follow-up examination six months later showed the patient able to work. The scar was somewhat tender, and there was occasional slight coughing.

CASE 11.—Female, 45 years old, with bronchial asthma for the past ten years, pneumonia, and pulmonary abscess. Drainage was instituted by resecting the second rib on the left side 10 cm. laterally from the bone-cartilage border on the anterior aspect. At a depth of 3 or 4 cm. there was a cavity about the size of an egg with lung sequestra and bronchial fistulas. Four months later a pedicled flap from the pectoralis major was implanted in a cavity half the size of a banana with residual fistulas. The wound healed in two weeks. Follow-up examination five months later showed the wound to have healed with a fine scar. A defect was seen in the chest wall which bulged upon coughing. The patient still had asthma with sputum.

CASE 12.—Male, 47 years old, underwent an operation for hernia. He had a pulmonary embolism and a pulmonary abscess. Six weeks after the herniotomy a puncture was done and pus was found. It was intended to institute drainage two months later, but no pleural adhesions were found upon resection of the eleventh rib, for which reason the operation was postponed. A month later the ninth rib was resected medially to the scapula. A cavity the size of an orange was found near the surface. There were lung sequestra and bronchial fistulas. Two months later a large part of the outer wall of the abscess was removed to permit better drainage. After three more months a pedicled flap from the latissimus dorsi was implanted

in a cavity about the size of the end of the thumb with fistulas. The wound healed in six weeks. Follow-up examination four months later showed the patient to have a slight cough. There was some reduction in the strength and mobility of the right arm. Some tenderness and a hyperesthetic area in front of the scar were noted.

CASE 13.—Male, 42 years old, with pneumonia and pulmonary abscess. Drainage was instituted with resection of the tenth and eleventh ribs as far back as possible on the left side. An abscess the size of a plum was found at a depth of 2 cm. Six weeks later there was a walnut-sized cavity with a bronchial fistula. A pedicled flap from the latissimus dorsi was implanted. The wound healed in two weeks. Follow-up examination four weeks later revealed the wound to have healed well.

CASE 14.—Female, 28 years old, with pneumonia and pulmonary abscess. Drainage was instituted by resecting the eighth, ninth, and tenth ribs on the left side 10 to 12 cm. anteriorly from the transverse process. An abscess cavity about the size of a fist with lung sequestra and bronchial fistulas was found at a depth of 0.5 cm. Two and one-half months later, due to rising temperature and increased sputum, another cavity above the first one had to be drained by resecting the seventh rib also. One and one-half months later still another small cavity between the two old ones was found and drained through the roof of the first cavity. Two months after the last drainage, a pedicled flap from the latissimus dorsi was implanted in an irregularly shaped cavity larger than an egg with bronchial fistulas. The wound healed in two weeks. Follow-up examination two months later showed the wound to be healed and the patient to be in good condition with no cough.

CASES 15 and 16.—Female, 39 years old, underwent a forceps delivery under narcosis and inhaled the contents of the stomach with development of pulmonary abscesses. Drainage was instituted by resecting about 7 cm. of the third, fourth, fifth, and sixth ribs on the right side anteriorly from the angulus costae. Broad drainage was used for two adjacent cavities fairly near the surface. Four weeks later a new abscess in the left lung also was drained by resecting the seventh and eighth ribs from the vertebral column anteriorly about 10 cm. A cavity the size of a walnut containing lung sequestra was found. Three months after the first operation a pedicled flap from the latissimus dorsi was implanted in the last cavity opened on the left side. The wound healed in four weeks. A pedicled flap from the latissimus dorsi was then implanted on the left side, also in a nearly walnut-sized cavity with bronchial fistulas. Complications developed. The primarily sutured wound suppurated and had to be drained, the amount of sputum increased to 225 c.c., and the temperature was high for a time. Furthermore, a bronchial communication developed. However, the wound was entirely healed five weeks after the operation. Follow-up examination one month later showed a well-healed scar, no cough, and improved general condition.

EDITOR'S NOTE: Apparently because of war conditions, it has been impossible to have the proof of this article corrected by the authors. The proof which was sent to Dr. Crafoord has not been acknowledged or returned. Accordingly, it seemed best not to postpone the publication of the article any longer, but to correct the proof here as best we could.

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NEUROFIBROMATOSIS WITH SARCOMAS IN THE LUNGS

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NEUROFIBROMATOSIS or von Recklinghausen's disease, with or without malignant manifestations, has been the subject of extensive study from the point of view of pathology, clinical picture, and therapy. Although Jones and Hart[1] report the removal of an intrathoracic neurofibroma for the relief of pressure symptoms, no record can be found in which a primary or metastatic malignant growth in the thoracic cavity has been the object of a surgical approach in a patient with neurofibromatosis. Furthermore, certain other points of interest have been observed in the case described below, which merit its recording in the literature. Since previous publications include complete bibliographies, reference is made only to relevant articles on the subject.

It is customary to think of neurofibromatosis as a disease of the cutaneous and subcutaneous tissues, with a definite hereditary factor predisposing toward the development of this condition. It has been claimed that neurofibromatosis is a manifestation of a developmental abnormality in the ectoderm and, as such, may be found in association with other congenital conditions such as retarded mental development, spina bifida, etc. There is certainly no generally accepted theory of the causation of neurofibromatosis; for the time being, the genesis of this condition remains as obscure as that of tumor formation in general. Endocrine dysfunction has been called upon to explain the formation of neurofibromas; some years ago Levin[2] reported the simultaneous presence of neurofibromatosis and endocrine disorders. However, there is hardly enough evidence at the present time to warrant the burdening of the already overtaxed endocrine organs with this additional pathogenetic role. Sharpe and Young[3] have pointed out the rather frequent relationship of puberty and pregnancy with early manifestations or with exacerbations of a previously existing neurofibromatosis. This again may be interpreted as the result of association with endocrine changes; but again one must emphasize the tenuousness of the alleged causal relationship.

Although neurofibromas are essentially benign tumors, malignant transformations have been noted. Hosoi[4] reported such an instance and also reviewed the literature on the subject of malignant changes in neurofibromas. Maksim, Henthorne, and Allebach[5] recently reported a case of neurofibromatosis with malignant thoracic tumor

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and metastases in a 12-year-old child. In the latter case, subcutaneous nodules had been present for four years. Autopsy showed a large, myxomatous, degenerated tumor which occupied almost the entire left thorax. The thoracic tumor on section proved to be a sarcoma. Small tumor masses were found in the adrenal glands; on section these were similar in histologic structure to the thoracic tumor.

CASE REPORT

J. B., a white woman, single, aged 29 years, was seen for the first time on May 28, 1939, complaining of pain in the left chest, nonproductive cough, weakness, and irregular fever of two months' duration. The onset of the illness was insidious, with progressive increase in all the symptoms. Medication had been prescribed but did not give relief.

Past History.—She had typhoid fever at the age of 5. Twelve years ago, at the age of 17, the patient noted the development of soft lumps on her forehead and chin. These were removed by her physician. Subsequently, other lumps of similar character developed on various parts of the body. These lumps were not painful or tender to the touch. Two years ago she suffered with severe pains in the abdomen and in both lumbar regions. She was sent to a hospital and a laparotomy was performed; two masses, said to have been situated in the retroperitoneal region, were removed. The pathologic diagnosis by the pathologist was xanthomatosis, but a re-examination at this time by one of the authors (M. L.) showed the lesions to be neurofibromas (Fig. 1).

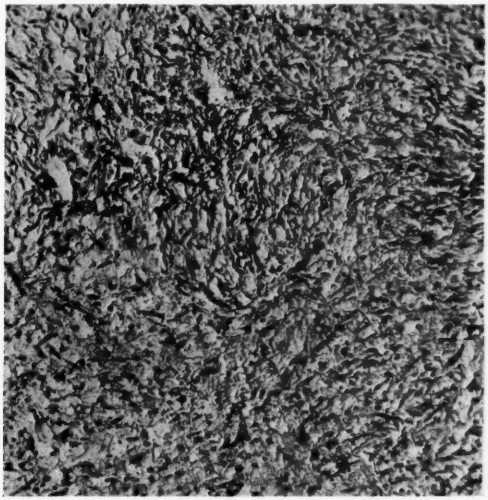

Fig. 1.—Retroperitoneal neurofibroma, with characteristic fibrillar structure.

Physical Examination.—The patient was a rather poorly nourished young woman who appeared chronically ill. The significant findings were confined to the skin and the thorax. Scattered over the arms, legs, back, and face were numerous soft, nontender, subcutaneous masses of varying sizes; the largest was about 2 cm. in diameter. Numerous small, soft, papillomatous masses were attached to the

skin of the trunk and upper extremities by narrow and broad pedicles. The skin was covered with irregular dark brown spots. Examination of the chest showed marked limitation of respiratory excursion of the left chest. The left lower chest was dull or flat on percussion, with marked diminution of breath sounds and absent tactile fremitus over the corresponding area. Occasional deep-seated medium râles were heard below the angle of the left scapula.

Cardiac dullness merged with the dullness of the left lower chest, and the left cardiac border could not be delineated on percussion. The right cardiac border seemed normal in position. The heart sounds were of good quality; the rate was increased (100); no murmurs were heard.

Examination of the abdomen revealed an operative scar in the left lower quadrant, but there were no masses or tenderness. The clinical impression at the time of this examination was neurofibromatosis and left pleural effusion, with possible underlying pulmonary neoplasm.

The patient was referred to The Jewish Hospital of Brooklyn and admitted to the surgical service of Dr. Henry Louria. The temperature was 101° F., pulse 120, and respirations 26. Otherwise, the findings were as detailed above. X-ray examination of the chest showed absence of illumination of the lower half of the left chest; a large round mass was noted in the right upper lobe region; a mass of similar character was present in the left upper lobe region close to the mediastinum (Fig. 2).

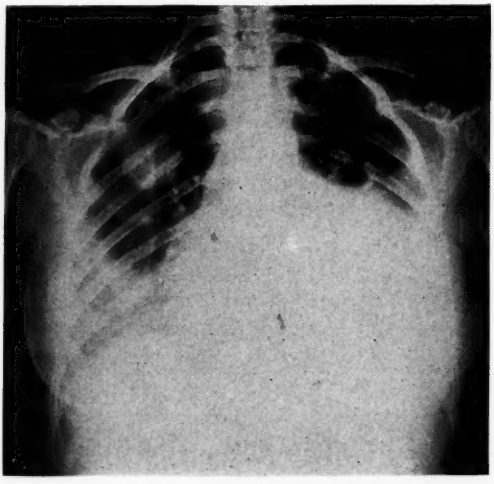

Fig. 2.—Roentgenogram showing opacity in the left chest and circular shadow in the right upper lobe.

Hospital Course.—During the first few days, the patient became more and more dyspneic and complained of unbearable pain in the left chest. On May 31, two subcutaneous nodules and one pedunculated growth were removed (Fig. 3). Sections from all three specimens showed them to be neurofibromas (Fig. 4). Because of severe discomfort and pain, it was decided to do an exploratory thoracotomy. On June 7, thoracotomy was performed in the seventh intercostal space in the posterior axillary line, and about 200 c.c. of a nonpurulent serosanguineous fluid were found. A curved incision over the seventh interspace from the vertebral region to the subaxillary line was made under local anesthesia; the pleural cavity

was opened. In the lower part of the upper lobe of the lung, a yellow-brown, tumorlike mass was visible, measuring approximately 10 cm. in diameter. After about one-half the mass had been liberated, the patient's condition suddenly became worse, her blood pressure dropped to 80/60, and the pulse became rapid and thready. It was, therefore, decided to discontinue the procedure and to conclude it at some other time. She reacted slowly, but satisfactorily, and on June

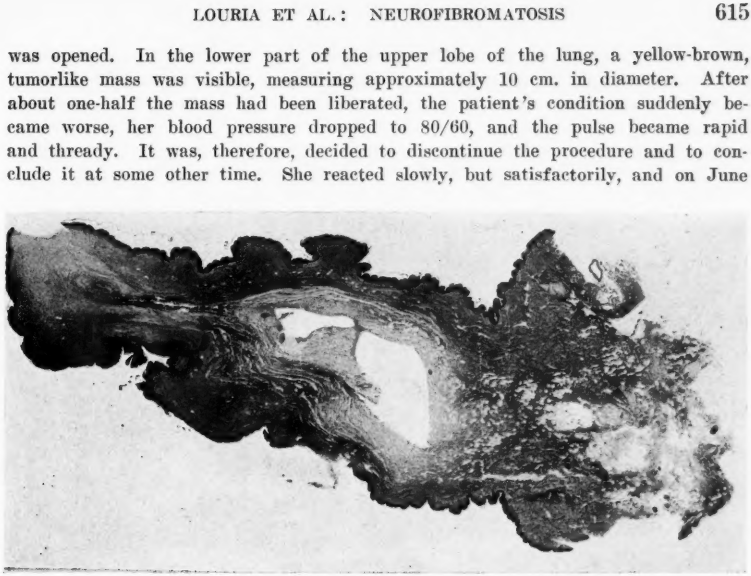

Fig. 3.—Papillomatous growth from the skin. (×8)

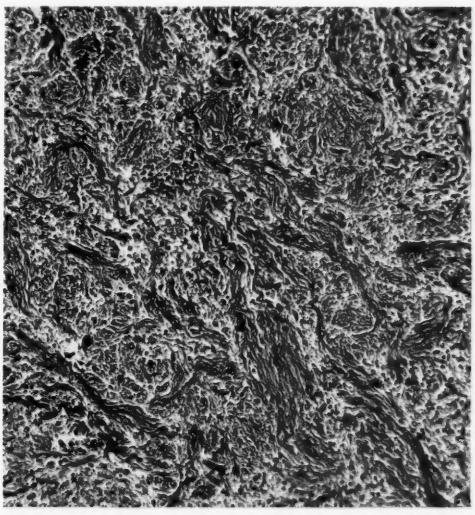

Fig. 4.—Section from tumor in the skin. Note the bundles of wavy fibers. (×150)

14, the old incision was opened under inhalation anesthesia. The tumor was now carefully separated without difficulty because it was well encapsulated, excepting in its mediastinal aspect. After removal of the main tumor mass (Fig. 5), several smaller fragments of the mediastinal portion were removed. Pathologic examination of this tumor showed it to be a sarcoma, the detailed characteristics of which were similar to the tumors subsequently found on autopsy and to be described below.

After operation, the patient was comfortable, and her general condition appeared to be markedly improved. The temperature dropped. The pain in the left chest diminished markedly, the respiratory distress was almost completely relieved, and the patient remained out of bed. On June 24, radiotherapy was instituted with the application of 4,000 R units to the right upper lobe. Following this, her temperature rose and remained elevated. After a few weeks she began to decline rapidly, vomiting bloody fluid, becoming drowsy and later comatose. She died July 13, one month after the last operation.

Fig. 5.—Tumor removed at operation. (One-half size)

Laboratory Data.—Cytologic examination of the pleural fluid showed a preparation consisting of many red blood cells with scattered lymphocytes and occasional large mononuclear cells. No cells of a malignant nature were recognizable. A culture was sterile.

Blood counts revealed the following:

				Polymorphonuclear Neutrophilic	
	Hemoglobin	Erythrocytes	Leucocytes	Leucocytes	Lymphocytes
5/28	67% (Haden-Hauser)	3,330,000	14,200	70%	25%
				Mononuclear Cells	
7/13	58%	3,100,000	9,200	5%	

A blood chemistry determination on May 29 showed total cholesterol, 160 mg. per cent, and urea nitrogen, 7.4 mg. per cent. The Kline reaction was negative. The sedimentation rate was 100 mm. per hour (Westergren method).

Cultures from the sputum yielded predominantly *Staphylococcus aureus;* no tubercle bacilli were found.

The clinical diagnosis was generalized neurofibromatosis and sarcomas of the lungs.

A post-mortem examination through an abdominal incision was performed two hours and thirty minutes after death. Only the important findings are described.

The body was that of a well-developed, poorly nourished, white female, 150 cm. long, weighing approximately 50 kg. The skin had a pale brown color and was dotted with many papillary projections up to 1 cm. in length which were attached

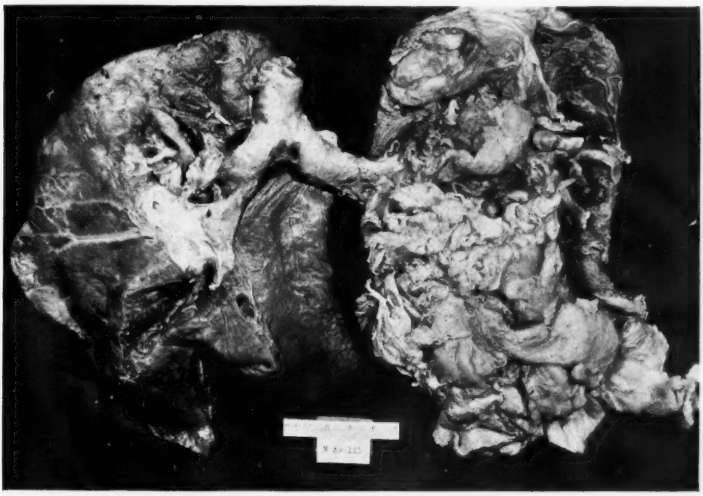

Fig. 6.—Lungs. Note the size of the tumor in the left lung and its lobulated structure.

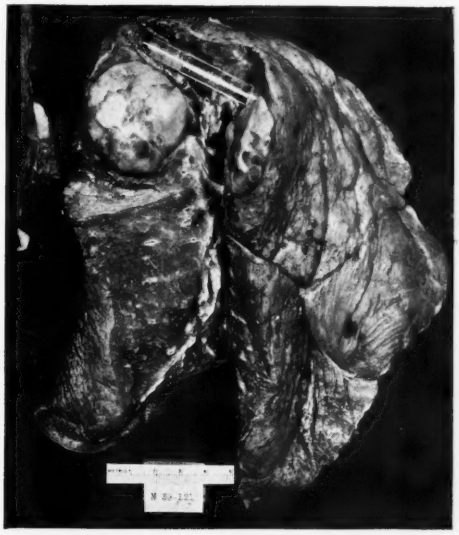

Fig. 7.—Section of metastasis in the right upper lobe. Compare this with Fig. 2.

by broad pedicles. There were also many flat, brown, pigmented areas scattered over the body, which were irregular in shape and in size. There was an operative incision over the left side of the thorax which was 16 cm. long, both angles of which

were opened for 2 cm. and 3 cm., respectively. There was a healed left lower pararectus scar 15 cm. long and two healed scars over the left buttock, measuring 2.4 cm. and 3.6 cm., respectively. The superficial lymph nodes were palpable in the left inguinal and in both axillary regions. On the right side, an irregular soft mass could be felt in the subcutaneous tissue of the forehead. The breasts were small and contained no masses. In the subcutaneous tissue of all the extremities, there were several well-circumscribed nodules, measuring up to 6 by 2 cm. The right pleural cavity contained no free fluid, and the pleural surfaces were smooth and glistening. The left pleural cavity was occupied by a large, white, soft tumor mass which was adherent to the parietal pleura, the diaphragm, and the pericardium and which was attached to the left lung (Fig. 6).

Lungs.—The pleura of the right lung was smooth and glistening. The surface of the upper lobe bulged and its consistency was firm. The lower lobe was crepitant throughout. On section, there was seen a well-circumscribed nodule situated in the upper lobe, measuring 4.5 cm. in diameter (Fig. 7). This nodule was composed of pearly gray tissue, mottled with yellow and red, and had a somewhat rubbery consistency. The entire left chest cavity was filled by a large lobulated mass of friable tissue which replaced the lower lobe of the left lung. The cut surfaces of this mass were gray, mottled with yellow, and contained extensive areas of hemorrhage. The upper lobe of the left lung was noncrepitant. It contained two well-circumscribed nodules, 1.5 and 1.8 cm. in diameter, which were similar to the nodule in the right lung. The tracheobronchial lymph nodes appeared to be somewhat enlarged. Their cut surfaces were black, mottled with gray. The mucosa of the trachea and bronchi was pink, gray, and glistening. The branches of the pulmonary artery were dilated. Lodged in the lumina were many obstructing, firm, friable, nonelastic, red-brown plugs. The periaortic lymph nodes appeared to be moderately enlarged and soft, and on section, they had a uniformly gray appearance.

A careful and extensive investigation of the abdominal cavity showed no pathologic masses. In view of the history of the exploratory laparotomy two years ago and the removal of tissue for pathologic examination, the retroperitoneal tissues were carefully examined for evidences of either recent or previous disease, and no abnormality could be discovered. The remaining organs showed no significant features.

Microscopic Examination.—Studies were made of sections taken from the tumor removed at operation and from the tumor of the left lung and right and left upper lobes removed at autopsy. They were fixed in formalin and Bouin's and Helley's fluids. Frozen sections were also made. Sections were stained by the hematoxylin-eosin, van Gieson, Laidlaw's connective tissue, Scharlach R, Masson's licht green, Masson's aniline blue, and Mallory phosphotungstic acid methods. With the usual stains the tumor was seen to consist of a wide variety of pleomorphic cells whose arrangement did not conform to any definite architectural pattern. The constituents were large spindle-shaped cells with spindle-shaped vesicular or hyperchromatic nuclei surrounded by a small rim of pink staining protoplasm. From many, fine delicate processes projected (Fig. 8). Numerous mono- and multinucleated bizarre-shaped giant cells were found; the nuclei were scattered indiscriminately in a large syncitial mass of deeply stained eosinophilic protoplasm. Many nuclei with mitotic figures were noted, and evidences of what appeared to be amitosis were also seen (Fig. 9). Between the cells could be seen a delicate reticular network of fibers which seemed to rise from the cells. In some places there was a resemblance to a cordlike arrangement, and interlacing strands of tissue could be recognized in others. Traversing the tumor were abundant capillaries filled with blood. Many extensive areas of hemorrhage and necrosis

were scattered throughout. With the Laidlaw stain (Fig. 10), an abundant stroma of very fine fibers formed a delicate network in many places. The connective tissue arrangement was confirmed with the Mallory and Masson stains.

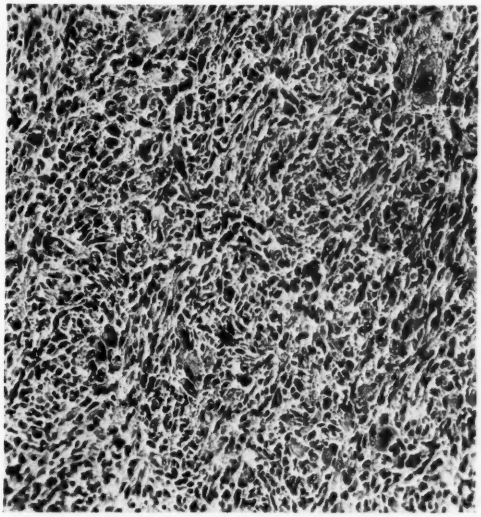

Fig. 8.—Section from tumor showing giant cells and spindle cells with fibrillae. (×170)

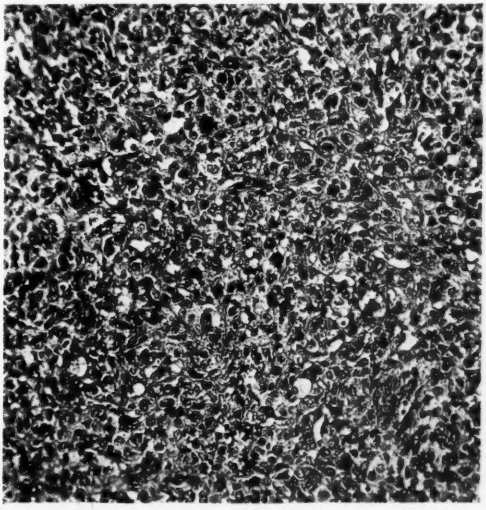

Fig. 9.—Photomicrograph showing lack of differentiation of cells; mitoses and hyperchromatism. (×250)

The *anatomic diagnosis* was: Neurofibromatosis in skin; sarcoma in lungs; dilatation of heart; thrombi in pulmonary artery; endarteritis of pulmonary arteries; congestion of viscera; infarcts in spleen and kidney (left); adenoma of

liver; cysts of kidney (left); cholesterosis of gall bladder; leiomyomas of uterus (subserous) and broad ligament (left); scar of laparotomy; absence of appendix; papillomas of skin.

Fig. 10.—Photomicrograph showing character of the reticulum. Laidlaw connective tissue stain. (×150)

DISCUSSION

The first point of interest in the reported case is concerned with the method of therapy. Why was an extensive surgical procedure carried out when there were obvious multiple masses in the lungs and the mediastinum? Why was radiotherapy not employed in place of surgery? The clinical reasoning which led to the adopted therapeutic regime was based upon the fact that the patient was obviously suffering from the mechanical effects of a large mass pressing on the heart and the mediastinal structures. Furthermore, the elevated temperature and tachycardia suggested active necrosis in the tumor. The radiotherapeutists advised that x-ray therapy would, in all likelihood, be of no avail, but would probably increase the patient's symptoms and hasten her death. On the other hand, it was felt that the smaller tumor masses might be radiosensitive and that x-ray therapy should be given a trial after removal of the large mass in the left thorax. Operation was admittedly hazardous, but was chosen as an alternative to standing by without offering the patient any chance of survival. The justification of the surgical procedure was seen in the patient's immediate postoperative course. After the removal of the large tumor mass, breathing became easier, and the patient stated that she

felt distinctly better. Jones and Hart[1] divided patients with surgical complications of von Recklinghausen's disease into three groups. This case properly falls into a combination of Groups 2 and 3 since the complicating tumor was malignant and also caused intrathoracic pressure symptoms.

The next feature of interest is the amazing rate of regrowth of the tumor. At operation, an enormous tumor was removed from the left chest. Density in the left chest on postoperative x-rays was interpreted as due to the accumulation of fluid; however, repeated attempts at aspiration yielded none. At autopsy, only six weeks after operation, the left half of the thorax was again filled with a solid tumor mass.

Concerning the relationship of the pulmonary sarcoma to the neurofibromas, one is hardly justified in making a dogmatic statement that the sarcoma resulted from the metastatic deposits of cellular elements derived from the subcutaneous tumors that had undergone malignant changes. The subcutaneous tumors were definitely neurofibromas; the pulmonary tumors were sarcomas. However, the simultaneous occurrence of both types of tumors in this case suggests a definite relationship. Furthermore, sarcomatous change in neurofibromatosis has been reported by Hosoi,[4] who asserts, from a review of the literature up to 1931, that in 13 per cent of all neurofibromas such transformation occurs. It is generally agreed that metastases arise from sarcomatous change in a single neurofibroma, the point of origin apparently being the connective tissue which surrounds the nerve fibers. Judging from recent work, reported by Tarlov,[7, 8] the origin of the malignancy from the Schwann cells is extremely doubtful. Penfield[6] expressed a similar point of view. In the cases reported by Maksim, Henthorne, and Allebach, the authors described cells which they allege are Schwann cells.

A study of this case suggests definite lines in the clinical management of neurofibromatosis. The tumors removed from the retroperitoneal region two years before the patient's death showed no evidence of local recurrence. It seems within the range of possibility that periodic x-ray examinations of the chest might have disclosed at some time later a single isolated tumor mass (similar to that found in the right upper lobe) for which lobectomy could have been attempted. This point of view receives support from a case history related by Maksim.[5] In that case a small shadow in the left upper chest was found upon x-ray examination of the chest. If a tumor mass in the abdomen is discovered, laparotomy is definitely indicated. An isolated tumor in the lung would justify lobectomy.

SUMMARY AND CONCLUSIONS

A case of neurofibromatosis with retroperitoneal lesions and metastatic sarcoma in the lungs is presented.

A pathogenetic relationship is suggested between the subcutaneous neurofibromas and the malignant visceral tumors.

Routine and periodic examinations of patients with neurofibromatosis may disclose visceral sarcomatous tumors at a stage in which operation may be of advantage.

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EVALUATION OF PULMONARY FUNCTION TESTS IN DETERMINATION OF RISK PRIOR TO THORACIC SURGERY

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INTRODUCTION

THERE is no greater problem in chest surgery than that of properly selecting cases for operation. To its solution should be brought clinical facilities, laboratory data, x-ray examinations, and such precision tests of function as may prove helpful.

Various respiratory function tests in relation to the surgical procedures of pneumothorax, phrenic crush, and thoracoplasty have been advocated as methods of precision giving information of value. The literature of cardiopulmonary function tests is so full of inconclusive observations that very critical analysis is necessary in order to draw any deductions worth while clinically.

For this reason, it has seemed wise here to confine ourselves to a critical survey of work done and results obtained with functional tests rather than to speak of all phases of preoperative selection. Therefore, I shall not dwell upon the well-known pathologicoanatomic indications and contraindications for collapse therapy, which are well understood.

VITAL CAPACITY

Since the determination of vital capacity was introduced by Hutchinson,[1] it has gone through several phases of professional acceptance. Thirty years were spent in correlations with anatomic measurements: height, weight, surface area, and chest expansion. High hopes were held that here at last was a sensitive indicator of incipient lung disease, but simple enough to be used by every practicing physician. Disappointments multiplied. The x-ray was discovered. Spirometers disappeared into attics at the turn of the century, and vital capacity literature for this period is fragmentary.

Interest revived in the 1910 decade, and the measurement was applied to soldiers as one test of physical fitness. The suspected influence of heart failure on vital capacity was amply confirmed. Standards for men and women were recalculated. Valuable work was done on vital capacity of children. Masses of data were accumulated trying to establish a quantitative relationship between various diseases and vital capacity. This interest has continued with sporadic intensification to the present time.

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That a diminution of vital capacity must occur as a result of certain lung diseases is well known. The introduction of this test into the clinic was founded upon the hope that these diseases might be quickly detected or their functional effect upon the individual accurately measured. The impossibility of realizing this hope gradually has become obvious. Lack of data prior to onset of illness has limited the usefulness of the test.

Arnett and DeOrsay[2] illuminate the situation by an apt analogy between vital capacity and weight determinations. Loss of twenty pounds' weight in a patient from a previous reading is much more important than the fact that he is found on a single reading to be twenty pounds under the average for his height. They examined one hundred college students of each sex for four years and concluded that the value of any particular reading depended upon a comparison with previous readings and whether deviations were greater than expected. It may be of diagnostic value in certain groups where interval examinations are possible, but it has little significance as an isolated observation.

Landau[3] believes vital capacity is affected by toxicity of tuberculosis as much as by mechanical factors because of observations of increased vital capacity after pneumothorax and after thoracoplasty, concurrent with subsidence of fever, reduction of sedimentation rate, and clinical improvement. Several instances are given in which thoracoplasty has had little effect upon vital capacity, supposedly proving that organs collapsed have been playing little part in respiration. Hutchinson's ability to anticipate the presence of tuberculosis before any of his colleagues could discover it by clinical methods then available is additional evidence in point.

Huckley[4] analyzed data on 2,500 college students and concluded that vital capacity is of little diagnostic value in relatively healthy young adults, because of multiple variables to be considered.

Louttit and Halford[5] could establish no valid relation between chest girth and vital capacity in insurance candidates, and they believed girth measurement to be overemphasized in insurance examinations.

Arnett,[6] investigating changes occurring in health and disease, found that successive readings give consistent values but have little similarity to theoretical values based upon surface areas. He presented figures of vital capacity before, during, and after acute bronchitis, influenza, and pneumonia, which are undoubtedly significant.

Kikuti,[7] notably among others, has found the ratio of residual air to total capacity after pneumothorax valuable in prognosis. The total capacity is said to decrease in proportion to the amount of air introduced in pneumothorax. In exudative tuberculosis, pneumothorax caused a decrease in vital capacity greater than the amount of in-

troduced air. Rise of the ratio of residual air to total capacity is supposed to indicate toxicity, poor response, or bad prognosis.

Thomas[8] also believes correlation between vital capacity and total capacity and residual air more important than vital capacity, but says that those measurements are very technical, difficult, and time-consuming.

Vital capacity values are based upon height, weight, chest circumference, stem length, and body surface. The combinations of these five variables run into large figures. Also, when actual vital capacity values of healthy people are compared with these theoretical standards, the deviations from each other and from the theoretical are very large. They indicate, to my mind, inadequacy of the standards as a basis for estimating respiratocirculatory reserve in an individual.

Lemon and Moersch[9] investigated the factors influencing vital capacity. Physical fitness is important; for instance, compare the high readings in a trained athlete and low readings in the same athlete after three months in bed with a broken femur. Muscle tone probably is the factor of most importance here.

Age has an indefinite effect, but there is a gradual decrease after 50, as emphysema, calcification of cartilages, atrophy of muscles, and general stiffening of the thoracic cage make their appearance.

Cardiac status naturally is a vital influence affecting the venous pressure, arterial saturation, etc.

Posture plays a large role, and Zoboli[10] presents statistical evidence to show that there is an increase in normal lung capacity by the simple maneuver of putting the hands behind the head. Muscle tone, fatigue, and respiratory quotient must be remembered as additional variables influencing the result in constantly changing ways as one examines successive individuals, or repeatedly examines the same individual.

Hamilton and Morgan[11] also have studied the effect of posture. They found a decrease in recumbent position, although the residual air remained the same. In complete inspiration, chest circumference may increase in recumbency. There was no vital capacity decrease while reclining if pressures slightly above diastolic level were applied to all four extremities just before lying down. The venous blood poured out of the extremities, therefore, may be the most important item in effecting the changes.

Budelmann,[12] too, found the vital capacity of normal man significantly increased after obstruction of the peripheral venous outflow. He claims this observation is a new proof that the amount of blood and the amount of air contained in the lung are inversely proportional to each other. Certain indications may be afforded for constriction of extremities in therapy of pulmonary edema and right heart failure, but only temporary relief would seem possible.

Banyai[13] thought he could avoid some of these variables by estimating vital capacity from roentgenologic chest volume. Films are taken, and the diameter of the patient's chest is measured in inspiration and expiration. The area of each film is multiplied by the corresponding diameter. The percentage ratio of expiration volume to inspiration volume normally is less than 70. Above 70 is considered suggestive of lowered vital capacity in patients with chronic pulmonary diseases, particularly emphysema. Others have supported his contention. However, the results can be altered considerably by thoracic or abdominal types of breathing.

Graham,[14] in 1920, proved that determination of vital capacity indicates the maximal opening in the chest wall compatible with life. His reasoning was as follows: Negative intrathoracic pressure must exist in at least some part of inspiratory effort, in order for the lungs to be filled. This depends principally upon the ability to enlarge the thorax. The degree of asphyxia which will follow creation of an open pneumothorax in a normal chest will depend upon the ratio of the amount of air which enters the thoracic opening to the amount which enters the lung at each inspiration. He gave a formula for computing the maximal compatible opening in the chest of a person able to maintain maximum vital capacity and emphasized the danger of early open drainage, especially if vital capacity is lowered too near to tidal air requirement. He demonstrated the reduction in empyema and the only gradual return toward normal, even after removal of exudate.

Graham's teaching had the practical effect of improving professional practice in the treatment of empyema.

Numerous experimental studies have examined the influence of physiologic alterations on vital capacity.

Beecher and Bradshaw[15] used a clever adaptation of Christie's[16] methods for measuring lung volume. They showed[17] that acute abdominal distention by air into the peritoneal cavity, stomach, or intestines causes a reduction in lung volume of from 20 to 30 per cent.

Lassen,[18] making serial determinations before and after operations, showed that "laparotomy lowers vital capacity in increasing degree the higher the incisions are in the abdomen. It is not influenced by extremity operations nor to any great extent by narcosis and anesthesia. Complications such as bronchitis, pneumonia, and infarct further lower the vital capacity according to the degree of their extent, and draw out considerably the period that elapses before the vital capacity again becomes normal."

He thus confirmed the 1927 work of Churchill and McNeil,[19] who compared postoperative vital capacity with preoperative readings and found large reductions.

One must remember exactly what the vital capacity measures: namely, the total amount of air that can be expired after a maximal inspiration. That is all. An extended list of factors acts efficiently to offset the admitted disadvantage of a lowered vital capacity. Among these should be remembered: (1) increase in the respiratory rate, multiplying three- or fourfold the tidal air movement before arousing consciousness of change; (2) greater pulmonary circulation, by means of increased rate and force of the heart beat; (3) elevated hemoglobin content of the blood, if anoxemia be chronic after pneumonectomy. In addition, Churchill[20] found an increased oxygen absorption in the remaining normal lung much greater than accounted for by greater ventilation, that is, by the use of capillary bed reserves.

Memory of these factors will serve as an anchor of reason. Brieger[21] found that, despite diminished vital capacity, the working ability of many patients is little below normal. He decided the working power of a patient could best be determined by a study of pulse and respiration, tachycardia being a characteristically bad sign. The vital capacity in health is a resultant of many components, and in thoracic disease it is additionally influenced by physiologic responses to the pathologic process.

As far back as 1926, Lilienthal[22] concluded that ability to work depended more upon heart condition than vital capacity, which is dependent upon too many variables to be important.

Lemon,[23] writing in 1930, quoted his own conclusions of 1924: "For routine purposes, the determination of the operative risk from the surgeon's opinion is probably on the whole a more satisfactory estimate than that obtained by means of the vital capacity readings." The value of experience was emphasized.

G. Nylin,[24] in 1933, developed a method for measuring the oxygen debt after work. The increased oxygen consumption after work was expressed as a percentage of the resting value. This value was used in estimating the function of the cardiopulmonary system in large numbers of presumably healthy and known cardiac persons, and standard values were established.

Nylin claimed ability to apply his cardiopulmonary function test to the measurement of relative oxygen debt, and, correlating with heart volume by x-ray, to be able to make an early diagnosis of impending cardiac insufficiency before symptoms of pulmonary or peripheral stasis have appeared.

Bluhm[25] applied Nylin's test to cases of tuberculosis with and without pneumothorax. He believed the test more informative than vital capacity determinations alone in estimating the patient's work tolerance.

The applications of these two men are in the right direction. They have tested the ability of the individual to do work in the simple

form of climbing over stairways. Their relative oxygen consumption calculation is based upon the fundamentally sound oxygen debt principle of Hill, Long, and Lupton,[26] which is known to be an indicator of physical fitness.

It is important to point out that a very bad impression of a patient might be obtained on the basis of oxygen debt tests, because of lack of training. Muscular training might change this apparent bad risk into a good risk. Every thoracic surgeon makes practical application of this fact when he tries to have his tuberculous patients up and about for a period before thoracoplasty. Whether one skilled in evaluating patients could not tell better the bad risk by observing the patient in the routine of living is a real question.

Extensive use of spirometry has been made in the study of emphysema. As a test of pulmonary ventilation, it has proved reliable in this disease. The results have been of interest to clinical investigators because the extent of disease and the response to re-education in breathing can be recorded. Since these observations also can be made with reasonable accuracy at the bedside, the spirometric evaluation of emphysema has had limited clinical application.

BLOOD GAS ANALYSIS

Michaud[27] was interested in arterial gases and found that carbon dioxide tension is so variable as to be unreliable. Oxygen tension in arterial blood tends to indicate gross pulmonary changes within a given age group, but is modified in the aged by emphysema, rigid thorax, and fibrosis.

He tried to classify patients, by means of the percentage saturations of hemoglobin, vital capacity, and total capacity tests, into three degrees of respiratory function. He concluded: "There exists a certain correlation between intensity of functional disturbance and extent of tuberculous lesions, but it is not rigid. The point which strikes those who study functional pulmonary disturbances is the variability, often disconcerting, of the results which are obtained." Oxygen and carbon dioxide dissociation curves are basic to an understanding of respiratory physiology, but routine clinical determinations are more burdensome than justified by information obtainable.

BRONCHOSPIROMETRY

Bronchoscopic spirometry is the simultaneous volumetric measurement and gas analysis of respiratory air from each lung separately. Advancement of the technique to present-day status is due to ingenious work done in the clinic of Professor J. Jacobaeus, principally by Frenckner and Björkman.[28] Although these workers are enthusiasts, they state that "the whole procedure is very trying to the patient." They have been alarmed to find isolated functions from lungs

quite different by bronchospirometry from those which would be concluded from physical and x-ray examinations. Björkman, therefore, defines the most important object of bronchospirometry to be "the determination of the function in each lung in cases of bilateral affection, in which an unilateral irreversible operation is contemplated."

An incidental finding from the associated gas analyses seems to me important: "The output of carbon dioxide from one lung has no connection with its intake of oxygen, but with its ventilation. When the volume of tidal air is great, and the oxygen intake is small, the output of carbon dioxide follows the ventilation. Therefore, there may be a considerable difference between the respiratory quotients in the right and left lungs." That is, a lung useless for oxygen intake may be playing a large part in ventilation and carbon dioxide output, or a totally useless lung may be compensated for completely by the opposite side. The futility of arterial gas analyses as a sensitive test of pulmonary function is apparent.

Lowered vital capacity favors retention of secretions and development of pneumonic complications. The findings of Björkman are of interest. He learned that badly diseased lungs obtain little benefit from cough, and only when secretions reach the carina, does the cough become effective in raising them. This apparent fact is explained on the theory that the extremely low respiratory current is of too weak intensity to aid cilia action and peristalsis in removing secretions. Jacobaeus[36] reports observing bronchoscopically such a patient in a violent fit of nonproductive coughing. The cough stopped when secretions, which had welled out of the diseased side, had been pushed back from the carina into the region from which they came.

Their finding that lungs well collapsed by pneumothorax often are assuming a major portion of the respiratory burden has forced a change in our older conception of absolute local rest with pneumothorax.

There is much information to be derived from bronchospirometry, which is making contributions of great theoretical interest. It has furnished statistical and actual proof of some facts generally accepted as true for a long time. I would be the last to minimize its investigative possibilities in solving the many problems remaining in respiratory physiology. Its use as a routine clinical procedure is still in the future. Clinical judgment usually can make an equally correct decision, particularly if seasoned with experience and common sense.

VENOUS PRESSURE

The venous pressure has interested numerous investigators more extensively in the early days of chest surgery than recently.

In 1930, Bosviel[29] declared that measurement of venous pulse in the course of artificial pneumothorax would disclose cardiovascular dis-

turbances and more clearly reveal cardiac compression than would measurement of the arterial pulse. Eyster[30] emphasized consistent elevation of venous pressure as a sensative indicator of slight cardiac failure.

Overholt and Pilcher[31] studied thirty-eight patients before and after operation. They found that unilateral elevations often were due to mechanical factors such as fibrosis and hydropneumothorax. Pressures frequently returned to normal after thoracoplasty which corrected the faulty mechanics. Elevations postoperatively were believed to indicate too extensive operation, these patients usually being functionally embarrassed. Three ribs removed rarely caused elevation; five or more frequently did. Additional evidence was thus obtained in favor of conservatism in ribs removed per stage.

Vasilesco[32] observed that peripheral venous pulse frequently is increased on the side of the lesion, after paralyzing the diaphragm by crushing or injecting phrenic nerves. This is not a constant finding, however.

Here lies the crux of the matter. The findings are not constant, and despite the simple technique required, venous pressure determinations have not been widely used.

ELECTROCARDIOGRAPHY

I have asked Dr. Edward Bland, one of our cardiac consultants, about the diagnostic and prognostic importance of the electrocardiogram in tuberculosis. He feels that the test is of academic interest only in this disease, showing merely what would be evident clinically.

Harbitz and Jervell[33] wrote in 1938: "In cases of [tuberculosis] the value of preoperative electrocardiography is so doubtful that it does not deserve a place among the standard methods of examination." As an indication of damaged myocardium or coronary disease, the electrocardiogram naturally has the same prognostic importance in lung surgery that it has in surgery of any other region.

BLOOD EXAMINATION

Secondary anemia is universally recognized as an untoward factor in the preoperative condition of any surgical patient. The recently introduced gravimetric hemoglobin determinations are important and worth while as methods of estimation. Iron therapy, of course, is very efficacious in relief of the simple hypochromic anemia commonly encountered. Comparison of consecutive sedimentation rate determinations and careful analysis of changes in differentially stained blood smears frequently will yield information of value in the preoperative selection of patients.

I have not mentioned the tests for vitamin deficiency, and I am not qualified to evaluate them critically, but empiric administration of

essential vitamins, in the diet and in concentrates, is essential to proper preparation of patients for elective surgery.

CONCLUSION

What, then, shall we say in conclusion? I approached this task of evaluating pulmonary functional tests sympathetically and hopefully. As a surgeon, I would sincerely like to know some simple test that would accurately predict a patient's ability to go through operations or to do work. But the confused and contradictory literature aptly presents the condition of the tests themselves, I fear. They are confused and contradictory. These numerous studies, designed to estimate the patient's ability to withstand strain, stimulate the thought that one can also estimate this capacity by observing his reactions to moderate exertion, and, in our experience, can estimate it more accurately.

I would not labor the argument that from the time a pulmonary or cardiac lesion appears, whether from bronchitis, carditis, tuberculosis, or coronary sclerosis, until clinical signs become evident, there are constant pathologic changes occurring in the organ involved. Some time usually passes, accompanied by changes in the direction of clinical symptoms, but these changes are, for the most part, undiagnosable by present methods. One must finally rely, then, upon the clinical evidence of organal insufficiency in recognizing the bad surgical risk, and this evidence rarely needs instrumental confirmation.

Without intending it so, the résumé seems to be a denial of the practical value of functional tests, as applied to sick people. This is the evidence as I have found it. On the other hand, the various tests have yielded, and may yet yield, much information of great value in problems of fundamental respiratory physiology.

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THORACOPLASTY IN THE TREATMENT OF PULMONARY TUBERCULOSIS

A Review of 100 Consecutive Cases

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During the past ten to fifteen years a great volume of literature has appeared dealing with thoracoplasty collapse in the treatment of pulmonary tuberculosis. In this communication it is not proposed to set forth new or original ideas concerning it, but rather to record our own experiences with a series of 100 consecutive cases. To complete the 100 cases, 245 thoracoplasty stages or operations were necessary. All operations in the series were performed by one of us (V. D. S.).

The type of case selected for this procedure is now fairly well standard in all chest clinics, and indications have been discussed and described so frequently that no lengthy description of them will be given at this point. Suffice it to say that the thoracoplasty case is usually one of advanced disease with cavitation, in which it is felt that control cannot be effected by the more minor procedures, or cases in which these procedures are impossible for various reasons. Our case selection will become apparent by referring to some of the tables to follow. However, possibly it should be mentioned that now we are accepting for thoracoplasty cases that only a few years ago would have been excluded. This exclusion would have been made either on account of the predominantly exudative nature of disease or on account of the extent of disease in the opposite lung. Today poorer risks can be treated successfully by using a multistage, graded procedure. Rather extensive disease in the better lung frequently can be brought under control by some form of collapse therapy, and then thoracoplasty can be carried out on the side containing the greater amount of tuberculosis. Bilateral collapse is used rather frequently at our institution, and, so far, there have been but few incidents meriting serious regret on our part. To be more specific, if a patient has a lesion in one lung that is too extensive to permit a major operative procedure on the opposite side with safety, and if he has in the other lung a lesion that requires thoracoplasty, pneumothorax is first established on the one side and thoracoplasty performed on the other. Various combinations of procedure are used.

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Our preoperative investigation includes a careful cardiovascular examination, complete hematologic studies, determination of the patient's vital capacity, venous pressure, and breath-holding time, augmented by bronchoscopy when indicated. We recognize the fact that the measurement of vital capacity necessarily does not indicate good or poor pulmonary function. To date we have not measured individual or combined pulmonary functions by the method described by Jacobaeus and others.

In regard to operative technique, it may be stated that we use no "routine" procedure. Each case is considered unto itself, and an operative technique is used that is considered most effective in that particular case. At our institution, we favor doing the least radical procedure consistent with good results. The location of the cavity or lesion is considered carefully, and then a technique which is as conservative as possible is applied.

For instance, if an apical cavity is peripherally placed, well away from the mediastinum, and not deep in the spinal gutter, no attempt is made to remove the transverse processes completely. The ribs are removed from the cartilages to the transverse processes, which, in such cases, will be found to be quite sufficient. If, on the other hand, the cavity is placed more medially, the transverse processes must be removed to effect closure. We believe that apicolysis should be added as infrequently as possible. Apicolysis prolongs the operation and adds shock and carries with it the well-recognized dangers of extrapleural tuberculous infection, cavity rupture, etc. Besides these dangers, we have found that frequently cavities are depressed to a lower level by the lysis and that more rib removal is necessary to effect closure than if the procedure had not been done. There are cases, however, in which cavities are large and placed very close to the mediastinum and deep in the spinal gutter, where closure can be expected reasonably only by the addition of apicolysis. When this procedure is indicated, we follow the method of Overholt and fill the created space with saline and close the wound completely.

In the poor risk cases we use the multistage operation, removing only one to two ribs at a time, with formalization of rib beds where operative delays are expected.

The type of anesthesia used in these cases was mostly avertin and nitrous oxide-oxygen, and despite the many objections to it, we have found it as satisfactory as any general anesthetic. The main objection to it, of course, is that the cough reflex is depressed markedly, and patients do not cough up sputum immediately after operation as well as they should, thereby increasing the danger of bronchiogenic spread. We have been fortunate, however, in that spread has occurred infrequently. Recently we have used high spinal anesthesia in ap-

proximately ninety cases* which are not included in this series, and so far we have been greatly pleased with its use. It does away completely with all the objections of general anesthesia, and, so far, no alarming incidents have occurred. The fullest cooperation of the patient can be obtained at all times.

Our present series consists of 100 cases treated by thoracoplasty for parenchymal disease. Included are twenty-six cases complicated by tuberculous empyema and two by a persisting pleurisy with effusion. The two latter were an oleothorax case and a pneumothorax case which would not re-expand following completion of treatment.

The age groups are listed in Table I.

TABLE I

AGES	NUMBER
15-19	9
20-29	43
30-39	32
40-49	16
	100

It is to be noted that the largest number is to be found in the age group of 20 to 29 years, and that 75 per cent of the patients operated upon were between 20 and 40 years of age. We have operated upon neither very young nor very old patients.

The classification of the disease at the time of operation is indicated in Table II.

TABLE II

STAGES OF DISEASE

STAGE		TOTAL	MALE		FEMALE	
			NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
Unilateral:	Minimal	1	0	0	1	1
	Moderately advanced	8	4	4	4	4
	Far advanced	26	10	10	16	16
Bilateral:	Minimal	0	0	0	0	0
	Moderately advanced	12	6	6	6	6
	Far advanced	53	34	34	19	19
	Total	100	54	54	46	46

From this table it will be noted that only thirty-five of the cases could be classified as strictly unilateral, while sixty-five of them had bilateral disease, in twenty-one of which contralateral collapse procedures had to be carried out. Of the whole group, 79 per cent were far advanced, while 20 per cent were moderately advanced.

Table III indicates the relative incidence of operation on the two sides of the chest in this series.

*This number has been increased to 170 cases, using nupercain solution 1:1,500 as the anesthetic agent.

TABLE III

SIDE ON WHICH THORACOPLASTY WAS CARRIED OUT

SIDE	NUMBER
Right	44
Left	56

In all cases there was or had been sufficient lung disease to require collapse for that purpose alone. However, as previously stated, twenty-six of these cases were complicated by tuberculous empyema, and two by pleurisy with effusion. The general indications for thoracoplasty in the series are shown in Table IV.

TABLE IV

INDICATIONS FOR THORACOPLASTY

	NUMBER
Parenchymal disease alone	72
Empyema + Parenchymal disease	26
Pleurisy with effusion + Parenchymal disease	2
	100

The type of disease present at the time of operation and its location and extent are shown in Table V.

TABLE V

TYPE OF DISEASE AND SIDE

	NONE	EXUDATIVE	MIXED EXUDATIVE PRODUCTIVE	PRODUCTIVE	TOTALS
Homolateral side	0 (0%)	25 (25%)	70 (70%)	5 (5%)	100
Contralateral side	35 (35%)	4 (4%)	32 (32%)	29 (29%)	100

In this table it will be noted that mixed exudative productive disease was present in the largest percentage on the operative side, while purely productive disease constituted only a very small number. In twenty-five of the cases, or 25 per cent, the disease was predominantly exudative on the operative side. In some of these cases, disease was actively extending at the time operation was undertaken. It is also to be noted from this table that in sixty-five cases disease was present in the opposite lung, again largely mixed exudative productive in type.

The method of control of the contralateral disease, where collapse control was considered necessary, is indicated in Table VI.

One case in the series received bilateral thoracoplasty for cavitation high in the apex of both lungs. Seventeen, or 17 per cent, had contralateral pneumothorax treatment, two had phrenics, and one had pneumothorax combined with a phrenic. It might be well to state here that nearly all our present phrenics are of the temporary type.

TABLE VI

CONTRALATERAL OPERATIVE PROCEDURES

	NUMBER
Thoracoplasty + Phrenic	1
Pneumothorax (including buffer)	17
Phrenic	2
Pneumothorax and Phrenic	1
	21

TABLE VII

RESULTS OF THORACOPLASTY ON CAVITIES, ACCORDING TO LOCATION

LOCATION OF CAVITY*	NUMBER	CLOSED	DECREASED	STATIONARY	LARGER
R_1	33	26 (78.8%)	5 (15.1%)	2 (6.1%)	0 (0%)
R_2	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)
R_3	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)
L_1	43	33 (76.7%)	8 (18.6%)	2 (4.7%)	0 (0%)
L_2	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)
L_1L_2	2	2 (100%)	0 (0%)	0 (0%)	0 (0%)
R_1R_2	2	1 (50%)	1 (50%)	0 (0%)	0 (0%)
R_1R_3	1	0 (0%)	1 (100%)	0 (0%)	0 (0%)
Total	83	64 (77.1%)	15 (18.1%)	4 (4.8%)	0 (0%)

*R_1, right upper lobe; R_2, right middle lobe; R_3, right lower lobe; L_1, left upper lobe; L_2, left lower lobe.

Table VII shows the number of cases with cavitation at the time of operation, their position, and the effect of operation upon them.

It will be noted from this table that cavity was present in 83 of the 100 cases. In seventy-eight cases cavitation was confined to one lobe; in five cases it was present in two lobes. Of the eighty-three cases, complete closure was effected in sixty-four, or 77.1 per cent, while fifteen, or 18.1 per cent, were decreased in size. In four of the cases, or 4.8 per cent, no decrease in cavity size was effected by the operation. For some of these a revision operation was necessary, as it was also in some of the cases which did not completely close. There were not enough middle and lower lobe cavities treated to state whether or not these are more difficult to close than upper lobe cavities. Special heavy penetration and Bucky x-ray plates are taken at a reasonable postoperative period to determine presence or absence of residual cavity.

The results of thoracoplasty according to the character of contralateral disease and the contralateral control measures used are listed in Table VIII.

TABLE VIII

RESULTS OF THORACOPLASTY ACCORDING TO CHARACTER OF CONTRALATERAL DISEASE AND CONTRALATERAL CONTROL MEASURES

STATE OF CONTRALATERAL LUNG	NO.	APPARENTLY CURED	ARRESTED AND APPARENTLY ARRESTED	IMPROVED	STATIONARY	WORSE	DEAD
No disease	35	3 (8.6%)	12 (34.3%)	15 (42.9%)	4 (11.4%)	0 (0%)	1 (2.8%)
Exudative	2	0 (0%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)
Mixed exudative productive	18	2 (11.1%)	6 (33.3%)	6 (33.3%)	0 (0%)	0 (0%)	4 (22.2%)
Productive	24	4 (16.7%)	10 (41.6%)	9 (37.5%	0 (0%)	0 (0%)	1 (4.2%)
Exudative + Pneumothorax	2	0 (0%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)
Mixed exudative productive + Pneumothorax	11	0 (0%)	3 (27.3%)	3 (27.3%)	0 (0%)	0 (0%)	5 (45.4%)
Mixed exudative productive + Phrenicectomy	2	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mixed exudative productive + Pneumothorax + Phrenic	1	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Productive + Pneumothorax	4	0 (0%)	3 (75%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
Productive + Phrenicectomy + Thoracoplasty	1	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	100	9	39	37	4	0	11

It will be noted from this table that no disease was present in the contralateral lung in only thirty-five cases, while disease was present in the remaining sixty-five. Of the sixty-five, it was sufficiently extensive or soft enough to require contralateral collapse in twenty-one cases. The end results with contralateral disease are indicated in another table. This table would indicate that contralateral disease is really no contraindication to thoracoplasty, provided it is not extensive or unstable, or that it is brought under control by some form of collapse. It is to be observed that there was little or no difference in the ultimate result whether contralateral disease was present or not. As shown, 85 per cent of both classes, i.e., with and without contralateral disease, showed definite improvement, whereas 50.8 per cent of the former and 43 per cent of the latter (without contralateral disease) were apparently arrested or apparently cured. Although five of the patients who had some form of contralateral compression died, we must remember that this measure was instituted in only the more seriously affected cases and so may be considered of very definite benefit in preparing the cases with bilateral disease for thoracoplasty operation. This table, of course, does not take into account the extent

and character of disease in the operated side. It would, however, indicate that we must consider the chest as a unit, and not as two lungs, when deciding upon collapse measures, and select aids to collapse diseased lungs and cavities no matter where they are located. Cavities must be closed regardless of whether they are situated in one lung or in both.

As previously stated, twenty-six of these cases were complicated by empyema. The result of thoracoplasty on the empyema component of the disease is shown in Table IX.

TABLE IX

RESULTS OF THORACOPLASTY ON TWENTY-SIX CASES OF EMPYEMA ACCORDING TO ORIGINAL CLASSIFICATION OF DISEASE

TYPE	NUMBER	COMPLETELY CLEARED	DIMINISHED	UNIMPROVED
I	1	1 (100%)	0 (0%)	0 (0%)
II	22	14 (64%)	8 (36%)	0 (0%)
III	3	0 (0%)	1 (33%)	2 (67%)
Total	26	15 (57.7%)	9 (34.6%)	2 (7.7%)

In this table the original classification of tuberculous empyema by Archibald is used although it is not our classification of empyema when considered or studied as an entity. Type I includes those cases of turbid fluid, not frankly purulent, but positive for tubercle bacilli.

Type II includes the thickly purulent, bacilli-positive cases, and Type III consists of those with mixed infection. This classification takes into consideration only the intrapleural disease and has no reference to the underlying lung condition. We have subdivided these groups to include underlying lung disease as follows:

Type I: Turbid positive fluid; lung disease controlled.
Type II: Turbid positive fluid; lung disease not controlled.
Type III: Purulent positive fluid; lung disease controlled.
Type IV: Purulent positive fluid; lung disease not controlled.
Type V: Mixed infected.

This classification was drawn up on account of the difference in treatment applied. In Type I it is seen that the lung should be re-expanded if possible and the pleural space obliterated to control the empyema. The same may be tried for a short time, with frequent washings, in Type III; in Types II and IV there is no question but that immediate thoracoplasty should be applied. The treatment of Type V depends upon many factors, and, as it is not proposed to discuss empyema in this paper, they will not be considered.

It will be noted from the table that of the three cases of Type III (Archibald) empyema, none were closed by simple thoracoplasty alone.

All required, or will require, secondary operating. The results in the other classes are relatively good. In fact a higher percentage of cures should be effected with the passage of time, as many of the cases had steadily diminishing amounts of fluid when this study was completed. Type III (Archibald) empyemas are, in the majority of incidents, the result of delayed treatment, and once they have reached this stage, they are very difficult to control. Treatment should be applied before mixed infection has had a chance to occur. This, of course, is not always possible, but in the majority of cases it is.

The ultimate results of operation in respect to operative risks are indicated in Table X.

TABLE X

ULTIMATE RESULTS OF THORACOPLASTY IN RESPECT TO OPERATIVE RISKS

RISKS	NUMBER	APPARENTLY CURED	ARRESTED AND APPARENTLY ARRESTED	IMPROVED	STATIONARY	WORSE	DEAD
Good	44	7 (15.9%)	19 (43.2%)	15 (34.1%)	3 (6.8%)	0 (0%)	0 (0%)
Fair	45	2 (4.5%)	19 (42.2%)	19 (42.2%)	1 (2.2%)	0 (0%)	4 (8.9%)
Poor	11	0 (0%)	1 (9.1%)	3 (27.3%)	0 (0%)	0 (0%)	7 (63.6%)
Total	100	9	39	37	4	0	11

In evaluating our risks, all factors are taken into consideration. The history of a good or poor resistance to disease holds a high place, as does also the status of the patient at the time operation is considered. The extent of disease, cavity size, etc., hold a lesser position of importance. Vital capacity, pulmonary function, blood picture, and the various laboratory procedures are all taken into consideration in evaluating operative risks and expected results.

In order for a patient to be considered a good risk, the disease must be unilateral or, at most, slight in amount and well fibrosed in the contralateral lung. The disease must be inactive and the patient's general condition satisfactory. The ten cases herein classified as poor risks were really desperate ones in which there was only a faint hope of saving life and restoring health by any procedure. It was accepted, therefore, as a last chance measure, and, as seen, the results were very unsatisfactory. Unfortunately, a relatively large number

TABLE XI

STAGES OF THORACOPLASTY

STAGES REQUIRED	NUMBER OF CASES
One	7
Two	44
Three	44
Four	4
Bilateral	1
Total	100

of our profession do not consider collapse therapy for their patients until this stage is reached, when the chance of saving life is small and the chance of being restored to health and usefulness infinitely smaller. With more recent improvements in technique, better results than those indicated in this table may be attained in the future.

The number of stages required in the various cases is indicated in Table XI. In Table XI are included:

Anterolateral stages	7
Apicolysis	7
Revision operations	5

It is believed now that in many of these cases too few stages were used in accomplishing the desired amount of rib removal. At the present time in the poor risk cases we are removing fewer ribs at one operation than we did previously, and already we feel that our results have improved and will continue to improve as a consequence.

The results of operation according to size of cavity are shown in Table XII.

TABLE XII

RESULTS OF THORACOPLASTY ACCORDING TO SIZE OF CAVITIES

A. Total cavities greater than 3 cm.	47	
Number closed	30	(63.8%)
Number decreased in size	13	(27.7%)
Number stationary or larger in size	4	(8.5%)
B. Total cavities less than 3 cm.	36	
Number closed	34	(94.4%)
Number decreased in size	2	(5.6%)
Number stationary or larger in size	0	(0%)

It is seen from this table that the smaller cavities were more easily and more frequently closed than the larger ones, which also holds true in other forms of collapse therapy. A considerable number of the large vomicae were so-called giant cavities, and doubtless, many of them were of the tension type, although at the time no investigation was carried out to determine this point.

TABLE XIII

RESULTS OF THORACOPLASTY ACCORDING TO CHARACTER OF CAVITY WALLS

CHARACTER OF WALLS	NUMBER	CLOSED	DECREASED	STATIONARY	LARGER
Thin	17	16 (94.1%)	1 (5.9%)	0 (0%)	0 (0%)
Moderately thick	38	28 (73.7%)	9 (23.7)	1 (2.6%)	0 (0%)
Thick	18	11 (61.1%)	4 (22.2%)	3 (16.7%)	0 (0%)
Pneumonic consolidation	10	9 (90%)	1 (10%)	0 (0%)	0 (0%)
Totals	83	64 (77.1%)	15 (18.1%)	4 (4.8%)	0 (0%)

The results when the character of the cavity wall is considered are indicated in Table XIII.

Again it is to be noted that the thinner the wall, the greater is the likelihood of complete closure. This also holds true in other forms of collapse therapy.

The comparison of mechanical results with clinical results is shown in Table XIV.

TABLE XIV

MECHANICAL RESULTS WITH RESPECT TO CLINICAL RESULTS

MECHANICAL RESULTS	NUMBER	APPARENTLY CURED	ARRESTED AND APPARENTLY ARRESTED	IMPROVED	STATIONARY	WORSE	DEAD
Good	73	8 (11%)	35 (47.9%)	28 (38.4%)	2 (2.7%)	0 (0%)	0 (0%)
Fair	25	1 (4%)	4 (16%)	8 (32%)	2 (8%)	0 (0%)	10 (40%)
Poor	2	0 (0%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)	1 (50%)
Total	100	9	39	37	4	0	11

In this table it is to be observed that a good mechanical result, i.e., satisfactory compression of the diseased area, does not always mean that the patient is free of symptoms or bacilli. The continuance of symptoms in some cases is due to tracheobronchial ulceration, which is not helped immediately by operation, and in some cases may persist for years. Bronchoscopy has shown persistence of this tracheobronchial disease after complete control of parenchymal disease.

It is to be noted also from this table that none of the cases with good mechanical results have died. Although in a certain number of cases some symptoms have persisted and some still have occasional positive sputa, yet all were improved. The ones that were not cured or arrested were converted from a state of "poor chronicity" to one of "good chronicity," or they may be expected to reach the cured classification with the passage of time. Poor mechanical results usually are due to delays in secondary operating for various reasons

TABLE XV

OPERATIVE PROCEDURES PRIOR TO THORACOPLASTY
OPERATIVE SIDE

None	41
Pneumothorax	23
Pneumothorax + Pneumolysis	11
Pneumothorax + Pneumolysis + Phrenic	2
Pneumothorax + Phrenic	7
Pneumothorax + Extrapleural pneumothorax	1
Phrenic	10
Oleothorax	4
Oleothorax + Phrenic	1
Total	100

causing postponement, such as spread of disease, general poor condition of the patient, wound infection, etc.

Many patients had received some form of compression therapy previous to operation. These procedures are indicated in Table XV.

TABLE XVI

RESULTS OF THORACOPLASTY ON TUBERCLE BACILLI

	NUMBER	PERCENTAGE
A. Thoracoplasty alone		
Patients with tubercle bacilli before operation	32	
Patients without tubercle bacilli after operation	23	71.9
B. Thoracoplasty combined with other operative aids		
Patients with tubercle bacilli before operation	38	
Patients without tubercle bacilli after operation	26	68.4

Although Table XVI is subdivided into two groups, thoracoplasty alone and thoracoplasty combined with other operative aids, it is doubtful if this is a true division. One must realize that in every case these other procedures were inadequate, and so it was necessary to resort to thoracoplasty as a final measure. In both cases, the percentage of sputum conversions is much the same. As mentioned before, failure to convert sputum from positive to negative does not mean that parenchymal disease has not been controlled. Many a postoperative positive sputum comes from tracheobronchial ulceration and the patient may be completely well and symptom-free except for slight cough. To determine if sputa are positive or negative three consecutive twenty-four-hour specimens are concentrated for direct examination, and also cultures are made. A series of such examinations are run several months apart. At our institution, stomach washings are not done at the present time, although the value of the procedure is well recognized. Like many other institutions, the large volume of work prevents the doing of many things of recognized value.

A word might be said here concerning extrapleural pneumothorax. At the time this thoracoplasty series was completed, only a very few of the former operations had been done, due to the fact that this procedure had been in use for a very short time. Since then, however, we have done more, and although some have been extremely satisfactory, many have had to have a superimposed thoracoplasty due to gradual obliteration of the extrapleural space.

The thickness of the pleura has a decided bearing upon the result of operation. The relationship of final result to pleural thickness as determined at the time of operation is indicated in Table XVII.

The comparison of cavity with noncavity cases is shown in Table XVIII. On the whole, the cavity cases did better than the noncavity cases, with the exception of the mortality rate. When the empyema cases were eliminated, however, the noncavity cases led by a good majority.

TABLE XVII

RESULTS OF THORACOPLASTY WITH RESPECT TO THE THICKNESS OF THE UNDERLYING PLEURA

	NUMBER	SATISFACTORY*	UNSATISFACTORY†
A. All Cases			
Thick and hard	75	43 (57.3%)	32 (42.7%)
Moderately thick	19	16 (84.2%)	3 (15.8%)
Thin and soft	5	5 (100%)	0 (0%)
Total	99‡	64 (64.6%)	35 (35.4%)
B. Parenchymal Disease Not Complicated by Empyema or Effusion			
Thick and hard	47	29 (61.7%)	18 (38.3%)
Moderately thick	19	16 (84.2%)	3 (15.8%)
Thin and soft	5	5 (100%)	0 (0%)
Total	71‡	50 (70.4%)	21 (29.6%)

*Tubercle bacilli negative, with cavity closed and in a better condition. Empyema cases were not considered satisfactory unless cleared completely.

†Tubercle bacilli positive, with cavity open; patient worse, or dead.

‡One case unknown.

TABLE XVIII

RESULTS OF THORACOPLASTY: COMPARISON OF CAVITY CASES WITH NONCAVITY CASES

PRESENT CONDITION, 1939	NUMBER	CAVITY CASES	NONCAVITY CASES
Apparently cured	9	8 (9.6%)	1 (5.9%)
Arrested and apparently arrested	39	33 (39.7%)	6 (35.3%)
Improved	37	29 (35%)	8 (47.1%)
Stationary	4	2 (2.4%)	2 (11.7%)
Worse	0	0 (0%)	0 (0%)
Dead	11	11 (13.3%)	0 (0%)
Total	100	83 (83%)	17 (17%)

The comparison of the cases that were sputum-positive with those that were sputum-negative is given in Table XIX. It will be seen that the results are slightly better in the sputum-negative cases, as might be expected. The fact that the results in this class are so little better, however, is somewhat surprising.

At our institution, we endeavor to carry out the operative stages at two-week intervals. If it is expected that delay will occur, the rib beds are formalized to prevent early regeneration. The results of thoracoplasty in those cases where delay occurred, but was not expected, are shown in Table XX.

TABLE XIX

RESULTS OF THORACOPLASTY: COMPARISON OF SPUTUM-POSITIVE AND SPUTUM-NEGATIVE CASES

PRESENT CONDITION, 1939	NUMBER	POSITIVE SPUTUM BEFORE OPERATION	NEGATIVE SPUTUM BEFORE OPERATION
A. All Cases			
Apparently cured	9	7 (77.8%)	2 (22.2%)
Arrested and apparently arrested	39	26 (37.2%)	13 (43.3%)
Improved	37	27 (28.6%)	10 (33.3%)
Stationary	4	1 (1.4%)	3 (10%)
Worse	0	0 (0%)	0 (0%)
Dead	11	9 (12.8%)	2 (2%)
Total	100	70 (70%)	30 (30%)
B. Parenchymal Disease Only			
Apparently cured	7	7 (11.7%)	0 (0%)
Arrested and apparently arrested	32	24 (40%)	8 (66.7%)
Improved	25	22 (36.6%)	3 (25%)
Stationary	0	0 (0%)	0 (0%)
Worse	0	0 (0%)	0 (0%)
Dead	8	7 (11.7%)	1 (8.3%)
Total	72	60 (83.3%)	12 (16.7%)

TABLE XX

RESULTS OF THORACOPLASTY WHEN STAGES WERE DELAYED

PRESENT CONDITION	LENGTH OF DELAY			
	ONE WEEK	1-2 WEEKS	2-4 WEEKS	4 WEEKS+
Apparently cured	3 (27.2%)	0 (0%)	0 (0%)	3 (21.4%)
Arrested and apparently arrested	4 (36.4%)	0 (0%)	1 (50%)	3 (21.4%)
Improved	2 (18.2%)	2 (100%)	0 (0%)	6 (42.9%)
Stationary	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Worse	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dead	2 (18.2%)	0 (0%)	1 (50%)	2 (14.3%)
Total	11	2	2	14

From Table XX A it is seen that when the delay was only one week, good mechanical results were obtained in nine of the eleven cases, with fair mechanical results in the other two. As the delay

TABLE XX A

RESULTS OF THORACOPLASTY WHEN STAGES WERE DELAYED

MECHANICAL RESULTS	LENGTH OF DELAY			
	ONE WEEK	1-2 WEEKS	2-4 WEEKS	4 WEEKS +
Good	9 (81.8%)	2 (100%)	1 (50%)	5 (35.7%)
Fair	2 (18.2%)	0 (0%)	1 (50%)	8 (57.1%)
Poor	0 (0%)	0 (0%)	0 (0%)	1 (7.2%)
Total	11	2	2	14

was lengthened to four weeks, or more, only five of fourteen cases had good mechanical results, while eight were fair. The longer the operative delay, the less the chance of a good mechanical result, which also lessens the chance of a good clinical result. All fair and poor mechanical results were not due to rib regeneration between stages. In some instances insufficient lengths of rib were removed at the time of operation. In other cases the patient did not cooperate in wearing compression appliances postoperatively.

The results of thoracoplasty according to activity of disease are shown in Table XXI. Cases that were clinically inactive at the time of operation showed a higher percentage of good results than the ones that were active. However, it seemed necessary in many instances to undertake operation despite this activity, other measures having failed to bring about control of disease.

TABLE XXI

RESULTS OF THORACOPLASTY ACCORDING TO TEMPERATURE MANIFESTATIONS

TEMPERATURE RANGE	NUMBER	SATISFACTORY*	UNSATISFACTORY†
All Cases, Including Empyema			
Not above 99°	73	54 (73.9%)	19 (26.1%)
99.2-100°	24	10 (41.7%)	14 (58.3%)
100.2+	3	1 (33.3%)	2 (66.7%)
Total	100	65	35
Parenchymal Disease Alone			
Not above 99°	55	42 (76.4%)	13 (23.6%)
99.2-100°	15	9 (60%)	6 (40%)
100.2+	2	1 (50%)	1 (50%)
Total	72	52	20

*Tubercle bacilli negative; cavity closed; condition stationary or better.
†Tubercle bacilli positive; cavity open; patient worse or dead.

The relationship of duration of disease to the results of operation is shown in Table XXII.

TABLE XXII

RESULTS OF THORACOPLASTY WITH RESPECT TO THE DURATION OF THE DISEASE FROM THE TIME OF DIAGNOSIS TO OPERATION

LAPSE OF TIME FROM DIAGNOSIS TO FIRST OPERATION	NUMBER	SATISFACTORY	UNSATISFACTORY
Less than one year	11	10 (90.9%)	1 (9.1%)
1-2 years	25	14 (56%)	11 (44%)
2-3 years	12	8 (66.7%)	4 (33.3%)
3-4 years	10	6 (60%)	4 (40%)
4-5 years	11	6 (54.5%)	5 (45.5%)
5-10 years	19	13 (68.4%)	6 (31.6%)
10-20 years	12	8 (66.7%)	4 (33.3%)
Total	100	65 (65%)	35 (35%)

Here it is seen that practically as good results can be obtained in the older cases as in those that have existed for a shorter length of time. This, of course, does not mean that the operation should be delayed when it is indicated, running the risk of progression and more advanced disease. It is to be noted that the best results were obtained in those patients whose disease existed for less than a year. We cannot say with certainty, however, that some of these would not have recovered without operation although at the time it was considered that thoracoplasty offered the best hope of recovery.

In this series there were eleven deaths. The causes of these deaths are listed in Table XXIII.

TABLE XXIII

CAUSES OF DEATHS

CASE NUMBER	DATE OF DEATH	TIME ELAPSED AFTER LAST STAGE	CAUSE OF DEATH
35	Jan. 30, 1935	8 days	Spontaneous pneumothorax; contralateral lung
48	Dec., 1937	17 mo.	Asthenia; progressive disease
57	Dec. 1, 1936	4 days	Postoperative cardiorespiratory failure
76	Jan., 1938	3 mo.	Influenzal pneumonia; progressive disease
80	Aug. 14, 1938	11 mo.	Progressive disease; diabetes
81	Sept. 24, 1937	7 days	Cardiorespiratory failure due to excessive reduction in vital capacity
84	Oct. 23, 1937	8 days	Cardiorespiratory failure
99	Sept. 25, 1938	7 mo.	Progressive disease
109	May 12, 1938	6 days	Cardiorespiratory failure
129	Jan. 8, 1939	4 mo.	Asthenia; progressive disease
130	Sept. 9, 1938	On table	Spontaneous pneumothorax; contralateral lung; postoperative

Of the eleven deaths, only six can be classified as operative deaths, giving a case mortality rate of 6 per cent. When the 245 stages are considered, the operative mortality is 2.5 per cent. Actually 11 per cent of our cases were dead within seventeen months after operation.

Serious complications are listed in Table XXIV.

TABLE XXIV

COMPLICATIONS	NUMBER	RECOVERY	FATAL RESULTS
Contralateral tuberculous spread	15	12 (80%)	3 (20%)
Homolateral spread	2	2 (100%)	0 (0%)
Homolateral + Contralateral spread	1	0 (0%)	1 (100%)
Contralateral spontaneous pneumothorax	2	0 (0%)	2 (100%)
Serious wound infection	5	5 (100%)	0 (0%)
Homolateral spread + Wound infection	1	1 (100%)	0 (0%)
Hemoptysis	1	1 (100%)	0 (0%)
Hemoptysis + Wound infection	1	1 (100%)	0 (0%)
Nontuberculous spread	3	2 (66.7%)	1 (33.3%)
Contralateral spread + Wound infection	2	1 (50%)	1 (50%)
Total	33	25 (75.8%)	8 (24.2%)

Contralateral spread and wound infection constitute the most serious of the complications. It is to be noted that contralateral spread occurred in fifteen cases, or 15 per cent, but twelve of these patients recovered. It is hoped, now that we are using spinal anesthesia rather extensively, that the number of these spreads will be reduced materially. The cause of spread, we believe, is due in the majority of cases to failure to cough up secretions immediately after operation, with resultant pooling in the opposite lung. With spinal anesthesia, the full cooperation of the patient can be obtained at all times. In this series complications occurred, mild or serious, in thirty-three cases, with recovery in twenty-five; eight died.

The present condition of the 100 patients is shown in Tables XXV A, XXV B, and XXV C. Table XXV A indicates the present condition of forty-one patients treated by thoracoplasty alone; Table XXV B, fifty-nine patients treated by thoracoplasty with other operative aids; and Table XXV C, the present condition of the whole group.

From a study of Table XXV C, it is to be observed that thoracoplasty has left something to be desired, as only nine cases can be classified as cured, while only forty can be classified as arrested, and thirty-six improved. However, as time passes, some of these cases will be

TABLE XXV A

PRESENT CONDITION OF 41 PATIENTS TREATED BY THORACOPLASTY ALONE DURING THE FOUR-YEAR PERIOD, 1934-1938 INCLUSIVE

CONDITION IN 1939	YEAR OF OPERATION AND TIME ELAPSED					TOTAL CASES
	1934, OR FOUR YEARS AGO	1935, OR THREE YEARS AGO	1936, OR TWO YEARS AGO	1937, OR ONE YEAR AGO	LESS THAN ONE YEAR	
Apparently cured	1	0	2	0	0	3 (7.3%)
Arrested and apparently arrested	0	1	5	9	4	19 (46.3%)
Improved	0	0	3	1	11	15 (36.6%)
Stationary	0	0	0	0	0	0 (0%)
Worse	0	0	0	0	0	0 (0%)
Dead	0	0	0	1	3	4 (9.8%)
Total	1	1	10	11	18	41 (100%)

TABLE XXV B

PRESENT CONDITION OF 59 PATIENTS TREATED BY THORACOPLASTY PLUS OTHER OPERATIVE AIDS DURING THE FOUR-YEAR PERIOD, 1934-1938 INCLUSIVE

CONDITION IN 1939	YEAR OF OPERATION AND TIME ELAPSED					TOTAL CASES
	1934, OR FOUR YEARS AGO	1935, OR THREE YEARS AGO	1936, OR TWO YEARS AGO	1937, OR ONE YEAR AGO	LESS THAN ONE YEAR	
Apparently cured	1	3	2	0	0	6 (10.2%)
Arrested and apparently arrested	0	1	5	7	8	21 (35.6%)
Improved	0	0	1	8	12	21 (35.6%)
Stationary	0	0	0	1	3	4 (6.8%)
Worse	0	0	0	0	0	0 (0%)
Dead	0	1	2	3	1	7 (11.8%)
Total	1	5	10	19	24	59 (100%)

TABLE XXV C

PRESENT CONDITION OF 100 PATIENTS TREATED BY THORACOPLASTY EITHER ALONE OR WITH OTHER COMPLEMENTARY MEASURES DURING THE FOUR-YEAR PERIOD, 1934-1938 INCLUSIVE

CONDITION IN 1939	YEAR OF OPERATION AND TIME ELAPSED					TOTAL CASES
	1934, OR FOUR YEARS AGO	1935, OR THREE YEARS AGO	1936, OR TWO YEARS AGO	1937, OR ONE YEAR AGO	LESS THAN ONE YEAR	
Apparently cured	2	3	4	0	0	9 (9%)
Arrested and apparently arrested	0	2	10	16	12	40 (40%)
Improved	0	0	4	9	23	36 (36%)
Stationary	0	0	0	1	3	4 (4%)
Worse	0	0	0	0	0	0 (0%)
Dead	0	1	2	4	4	11 (11%)
Total	2	6	20	30	42	100 (100%)

promoted to higher grades. On the other hand, only four were not improved by operation, and eleven died following it. That is, the operation was unsatisfactory in fifteen cases, or in 15 per cent. In all

fairness, it should be pointed out that many of the cases classified as improved are as well as those classified as arrested or cured, but occasional positive sputum keeps them from the more favorable classes. As previously mentioned, this occasional positive sputum often is due to tracheobronchial disease and not to failure to control parenchymal disease. Many of these cases, it is felt, will become negative eventually, as many of them now are for long periods of time.

Many of these patients, too, had very extensive, and in some instances bilateral, disease, which has a decided bearing upon final results. Unfortunately, it is not often that we are presented with cases which we can group as "good chronics" of the original Archibald classification.

RENAL FAILURE AS A COMPLICATION OF CARDIAC TAMPONADE

With Report of a Case

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IN RECENT years notable progress has been made in the diagnosis and treatment of heart wounds. The diagnosis of typical acute compression of the heart (cardiac tamponade) is not difficult for the surgeon who will remember the triad emphasized by Beck,[1] namely, low arterial pressure, high venous pressure, and a small quiet heart. Cardiac tamponade must be diagnosed and treated promptly, but there is not full agreement as to the methods of treatment. Bigger[2] advises conservative treatment for those patients who have cardiac tamponade when the symptoms respond to supportive measures such as the administration of drugs, external heat, and intravenous fluids. He performs pericardial paracentesis in these cases and does not operate unless the intrapericardial bleeding persists. In those patients whose symptoms do not respond to supportive measures, Bigger advises immediate operation. Elkin[3] prefers to operate immediately in both types of cases. There has been much discussion of the danger inherent in performing pericardial paracentesis, since the point of the aspirating needle may injure a coronary vessel or the heart muscle. At least one instance of death due to such a mishap has been reported.[4] The risk is minimized, however, if the surgeon is prepared to operate immediately should the intrapericardial bleeding persist after aspiration has been performed. The possibility that complications other than death may result from prolonged acute compression of the heart was mentioned by Blalock in discussing Bigger's paper.[2] The following case report describes the occurrence of one such complication.

J. S., unit 165590, a 27-year-old negro, was brought to the accident room of the Johns Hopkins Hospital by ambulance at 9:15 P.M. on March 11, 1939. He was unconscious, cold, and the radial pulses were imperceptible. His clothes were blood-soaked. There was a small stab wound beneath the left clavicle at the sternal border, over the second intercostal space. This was bleeding moderately. All observers thought the patient moribund. The time interval between injury and arrival could not be ascertained as there were no witnesses available. A pressure bandage was applied to the wound, the foot of the stretcher elevated, external heat applied, and an intravenous infusion of 5 per cent glucose begun. He was given coramine intramuscularly. The heart sounds were faint and distant, and the rate counted at 100 to the minute. He was breathing deeply, but not rapidly. All observers remarked upon the absence of dyspnea and cyanosis. There was no

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evidence of pneumothorax or hemothorax. Following the administration of one liter of glucose, radial pulses could be felt. The systolic blood pressure could be measured at 40 to 60 mm. of mercury. The pulse rate varied between 110 and 130. His radial pulse became imperceptible about two hours later, and a second liter of glucose was administered intravenously. The systolic blood pressure came up to 60 mm. of mercury. The wound was sutured, tetanus antitoxin administered, and the patient moved to the ward. He was now conscious and somewhat restless. During the remainder of the night his condition was about the same. The radial pulse was weak but easily counted at 100; the respiratory rate was 24 to 30; the systolic blood pressure varied between 60 and 80. He took fluids well by mouth. We did not give him further intravenous fluid or blood as we felt that raising his pressure might cause further bleeding. He was considered to have a wound of either the great vessels, the left subclavian, or the left internal mammary vessels.

At 9 A.M. the following day the patient's radial pulse again became imperceptible, and his blood pressure could not be measured. It was remarkable that the patient had a hemoglobin determination of 86 per cent at this time. Difficulty was experienced in matching the patient's blood for a transfusion, so intravenous glucose was then administered. At first his condition improved, and the systolic blood pressure rose to 50 mm. of mercury. However, very shortly after the infusion was begun the patient became extremely dyspneic. Examination of his chest failed to reveal abnormal signs over the lungs, but the area of cardiac dullness was thought to be abnormally large. The venous pressure was then measured and found to be 200 mm. of saline. The diagnosis of cardiac tamponade was now made, and pericardial paracentesis was performed immediately. From the pericardial sac was aspirated 140 c.c. of dark blood. The immediate improvement in the patient's condition was striking. The respirations became slower in rate and deeper, the systolic blood pressure rose to 90 mm. of mercury, and the venous pressure fell to 100 mm. of saline. This was about fifteen hours after injury. His condition remained good. In the evening it was noticed that the patient had not voided in twenty-four hours despite a fluid intake of 8,600 c.c. by all routes in the same period. His bladder did not seem distended. He had, however, perspired profusely for many hours and had twice vomited small amounts of fluid.

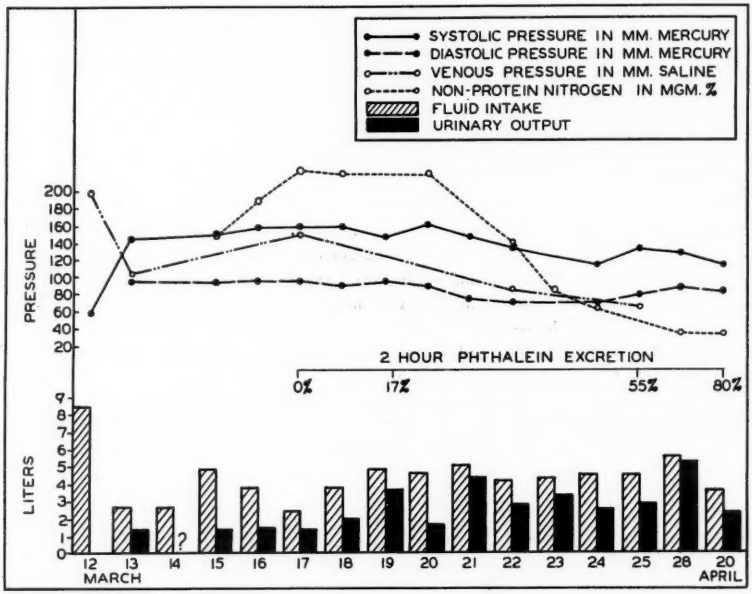
The next day the patient seemed to be in excellent condition. His blood pressure was 146/96, an increase which is significant in view of later developments. His recorded pulse was 100, respirations 26, temperature 100° F. The hemoglobin had fallen to 70 per cent. There was definite cardiac enlargement, confirmed by x-ray examination. The lungs were clear. He did not void and at noon was catheterized, 1,000 c.c. being obtained.

The following day, the third following admission, his condition remained the same. Again the urine output remained low. On the fourth day blood chemistry determination revealed an elevation of the nonprotein nitrogen to 148 mg. per cent. Other findings were normal. His pulse rate was 60, respiratory rate was 18, and he was almost afebrile. A retention catheter was inserted into the bladder, and intravenous glucose was administered. Urinalysis now showed erythrocytes, leucocytes, casts, and albumin. The blood pressure was 152/96, and the hemoglobin had fallen to 62 per cent.

During the next several days the patient continued to exhibit signs of renal failure. The urinary output was low, the blood nonprotein nitrogen rose to 220 mg. per cent, and the urine was grossly bloody. The patient's blood pressure remained nearly constantly at 160/95. Phenolsulphonephthalein was administered intravenously, and only 17 per cent of the dye excreted in the urine in two hours.

Dilution-concentration test indicated diminished concentrating ability. The patient was drowsy. A pericardial friction rub and enlargement of the liver were observed. The hemoglobin fell to 50 per cent. The patient then contracted a beta hemolytic streptococcal throat infection which was followed by right otitis media, necessitating myringotomy. He was given sulfanilamide.

The patient's condition began to improve on the tenth day following admission. There were coincident decreases in blood nonprotein nitrogen level, blood pressure, and albuminuria, and increase in urinary output. The upper respiratory infection responded to therapy.



J.S. UNIT #165590 MALE NEGRO WA.R. NEGATIVE

Fig. 1.

One month after admission the patient was afebrile. The hemoglobin was 70 per cent. The patient's blood pressure reading was 116/80. The blood nonprotein nitrogen was normal, urinary output good, and the urine clear. The phthalein excretion was now 80 per cent in two hours. Dilution-concentration tests and urea-clearance were satisfactory. The patient was discharged April 21, 1939, forty-one days after having been stabbed. His heart sounds were normal, and there was no evidence of renal damage.

In summary, this was a patient who suffered from acute compression of the heart which was undiagnosed until at least twelve hours after the wound was inflicted. Ultimate recognition and treatment of the cardiac tamponade prevented the death of the patient. As an immediate complication the patient developed acute renal failure. The evidences of renal damage and dysfunction persisted after the circulatory system

in general had recovered, but finally the kidney function became perfectly normal. The renal failure was probably not related to the respiratory infection since the infection did not appear until several days after uremia had been present. We feel that we are correct in believing that the renal failure in this patient would not have occurred had the acute cardiac compression been recognized and treated promptly.

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MECHANICAL AIDS TO COLLAPSE THERAPY

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INTRODUCTION

METHODS to produce change in the contour or mobility of the thorax have been suggested repeatedly during the past forty years. Devices and postures have been invented to apply to various parts of the chest and abdomen, both in the intact tuberculous patient and in the postoperative subject. The necessity for such procedures is not widely recognized, and their effect often has not, or cannot, be proved.

The methods have varied with the objectives. If an elevation and decreased motility of the diaphragm was desired, an abdominal belt, binder, or brace was applied. If a depression, fixation, or immobilization of an area of the chest wall was desired, a binder, vest, padded harness, metal brace, adhesive strap, plastic weight, sling, plaster mold, pneumatic or elastic jacket, postural pressure, or connection to a frame was arranged. Strapping or plastic weights have been used to prevent paradoxical movement of the chest wall. Mobilization of the shoulder, scapula, or muscles has been induced after operation by the use of active or passively effective pullers.

The chronology of these orthopedic measures is interesting. Although many have been described during the past fifty years, they follow a few simple principles. We have reviewed the suggestions of about forty clinical groups, and the similarity of their devices can be seen. Some groups have changed from one device to another, while others use several different measures at one time or when indicated.

HISTORICAL

In 1898 and 1902, Denison reported the use of an adhesive tape chest binder in nonsurgical cases. Tapered straps were applied from the axilla on the involved side to a contralateral shoulder girdle. Sewall and Swezey used adhesive strapping around the chest at the axillae before 1921; Golden used it before 1923, Wingfield in England used it repeatedly at one base, and Lilienthal, in 1925, first recommended the use of an elastic webbing, anchored by adhesive, for nonsurgical and post-thoracoplasty chests.

In 1911, Sauerbruch and Schumacher mentioned briefly the use of a harness after thoracoplasty. In 1925, Gravesen described in a British text his "bandage" harness; Oelgoetz in Germany described a "harness splint"; and, in 1932, Woodruff published data on his "thoracoplasty brace" or harness.

In 1916, Webb, Forster, and Houck suggested the use of lateral posture and an axillary pillow at night by patients at bed rest. In 1933, Bisgard used the same

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lateral posture with a bolster after thoracoplasty, and he called it "wedge compression" therapy. It has been part of the postoperative routine reported by several clinicians since that time.

In 1917, Porges, in the German literature, reported the use of a chest binder in nonsurgical cases. Sewall and Swezey gave more details in 1921 of a similar belt binder. Beasley, in 1922, also described such a padded binder for the lower chest, and in 1924 Young reported use of an "apex belt" in England. In 1924, Edward Welles used a harness belt around the chest after lower stages of thoracoplasty. In 1937, Dayton (reported by Urquhart) used a wide binder with pads in the areas collapsed by thoracoplasty, and in 1938 Wangensteen, Carlson, and Bowers described a less extensive, but adjustable, binder. The postoperative use of a binder is seen to be derived from its use in patients treated without surgery.

In 1922, Levitt described an encircling plaster cast to be applied to the lower chest after thoracoplasty. In 1923, Sayago in Spain applied a plaster cast to the whole chest, with an anterior window on the side contralateral to operation. In 1925, Howell described anterior and posterior connected molds for the unoperated hemithorax. The use of plaster has not been reported recently, however.

Abdominal belts were first reported in 1922 by H. Alexander and Kountz, who used a cloth belt, with a pad and spring above the symphysis pubis. In 1934, Gordon and Meakins and Christie recommended the use of cloth belts or binders in nonsurgical cases with emphysema. Brock and Woodson obtained elevation of the diaphragm and a decrease of symptoms by elevating the foot of the bed on blocks.

In 1923, several devices were described. Golden used a cloth vest containing a pneumatic pad for splinting one side of an intact chest wall; Stewart in England used a "lung splint," or adjustable brace on nonsurgical cases; and Kisch in Germany used a large metal brace after thoracoplasty.

In 1931, Roberts and Nelson in England reported using a post-thoracoplasty brace. A. B. Steele described a padded metal brace for nonsurgical cases in 1937, and John Steele of Wisconsin, in 1939, reported the use of a padded spring brace for localized pressure.

Suspension of the patient in a sling, with the body weight on the involved hemithorax, has been reported several times. Davis reported a hammock in 1928, and Weeks and Delpratt used a sling from a balkan frame before 1932.

Plastic weights have been used for years, but perhaps have seemed too simple to report. Gravesen, before 1925, used shotbags weighing from 11 to 13 pounds. Edwards, also in England, used bags varying in weight from 6 to 24 pounds. John Alexander and others have found them useful. They have been applied to intact chests and to the decostalized area after thoracoplasty. In addition to compression and immobilization, they have at times been used to decrease paradoxical mobility. In 1934, O'Brien attempted to control paradox by strapping the upper arm to the contiguous chest. Urquhart reported the use of 15-pound sandbags applied to the hemithorax after operation. The Trudeau group experimented with the effect of a shotbag on the abdomen below a paralyzed diaphragm.

Photographs or drawings of most of these devices have usually appeared with the original description and are quite graphic. Unfortunately, they cannot be reprinted extensively here.

THEORETICAL

In evolving the present program of mechanical aids used on the Thoracic Service of the Wisconsin General Hospital, we have been guided by the need for obtaining certain results and by the qualities of the proposed devices. Without

any doubt, the greatest requirement for the successful collapse of a disease process is a carefully planned and executed series of operations; all adjuvants are definitely secondary, and may, in turn, be hampered by incomplete surgical efforts.

The routine used after thoracoplasty must include methods to be applied in several situations. The correction and prophylaxis of scoliosis must begin shortly after operation, and the method used must be simple, capable of early and constant application, and must be well tolerated. Paradoxical movement of the decostalized chest wall may require immobilization by a painless method which can be applied early and will not increase the work of respiration. Compression and immobilization of the chest wall in a collapsed position after operation will require constant pressure by a device which can be applied easily to the individual patient, which is well tolerated, and which will have a minimal cost. Whether the device must produce an effect over a small or large area will depend upon the extent of the operations. Mobilization of the shoulder and scapula and the stretching of tense, shortened, and atrophic muscles may require a method which can be repeated painlessly, without assistance, and without undue traction on the depressed chest wall.

PRACTICAL

The methods which we have used to meet these situations will be described and illustrated.

Scoliosis.—Some degree of lateral spine curvature occurs almost invariably. It is often so severe in the cervical region that the patient seems to be constantly peering around a corner. Many methods have been used to prevent the deformity, including braces, jackets, traction,

Fig. 1.—Sandbag for prevention of scoliosis.

and even osteosynthesis. One of the objects of Bisgard's lateral posture over a bolster was correction of the scoliosis, and it has since been widely used. A note of discord has recently sounded regarding its efficiency, and Welles, Wangensteen, and others do not feel hopeful of

its effect. It seems to be theoretically sound, but practically, in our hands, it can be used only a few hours a day; it has been poorly tolerated, it cannot be used in cases with complications, and the results have been unsatisfactory.

We have used the wedge compression regularly for several years, and have also tried celluloid jackets, traction by horizontal slings, and other means. Eight months ago an attempt was made to deflect the head and neck toward the thoracoplasty side by placing a 15-pound oblong sandbag next to the head beneath the pillow (Fig. 1). Since then, it has been used in fifty cases. It is too early to predict the results of this simple method, but so far they are remarkable. Most of the spines are straight, and only mild scoliosis has occurred in any case. The bag may be put in place the day after operation and may be used twenty-four hours a day; it is not painful, and complications do not contradict its use. It may be anchored to the head of the bed and replaced repeatedly against the head when necessary. It lacks the compression effect of the bolster, but that is supplied by other devices.

Paradoxical Movement.—It has been found that contrary chest wall movement has been notably reduced by apicopexy (fixation of the depressed apex) in operations which include an apicolysis. Varying degrees of paradox may occur, however, after simple paravertebral first stages or after second stages.

At present, two methods are used to minimize its effects, which may be not only painful, but exhausting. Gentle, but firm, pressure is first applied to the area for a test of effect. If this is helpful to breathing or coughing, a 2- to 4-pound shotbag is applied. This may be anchored to a neck girdle or to the bed. The patient may steady it to prevent bouncing while coughing.

If the movement is gross, a padded harness (to be described) is applied for a trial of its effect. It has given good relief in several cases.

A third method is now being developed in which the hemithorax is surrounded by a sealed metal chamber and a negative pressure is used to prevent the paradox. The preliminary problems are being solved satisfactorily.

A Drinker respirator has been used in two cases, unsuccessfully because of unrelated complications.

Mobilization of Shoulder Structures.—Two methods are in use at present. In one, a knotted gauze rope is tied to the corner of the bed on the side of operation. The ordinary patient (with no muscle atrophy, a rapid recovery, and scant pain) can use this active method to move gradually the muscles, shoulder joint, and scapula, beginning from five to ten days after each stage. For those who are asthenic and have pain, a passive mobilization can be produced by a rope-and-pulley device which is attached in the same manner (Fig. 2). One of these devices has been used on all cases for the past two years.

Compression and Immobilization of the Chest Wall.—The progress from one device to another which has occurred in our wards in the past several years is probably similar to that in any clinic working on the same subject. The results may be different, however, and worth describing.

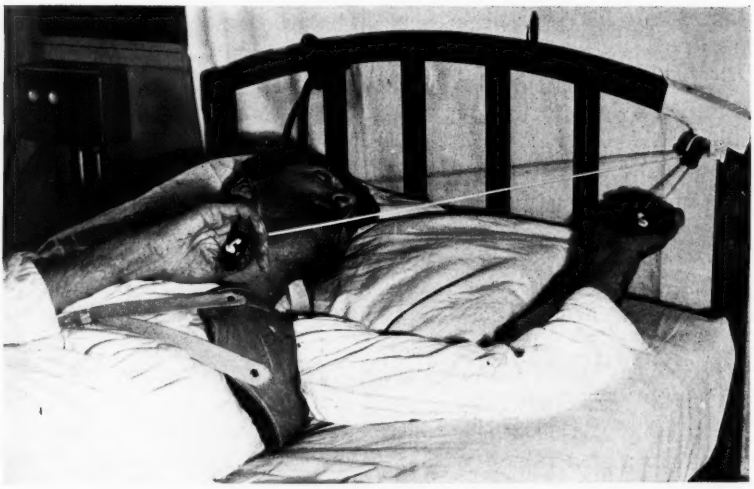

Fig. 2.—Puller for mobilization of shoulder.

Lilienthal found most braces too bulky and cumbersome. To his objections might be added the terms "uncomfortable and expensive." He also warned against encircling the chest, with a resultant loss of lung function and increase in respiratory work.

The first experiments were made with a padded hammock slung from a balkan frame. This method was poorly tolerated, inconstantly applied, and inconvenient. It was used in only three cases, each of which had had extensive lower rib resections.

The second device was the ordinary canvas binder with pads. This consisted of a strip of canvas 10 inches wide and 40 inches long. Four straps were attached to one end and four buckles to the opposite end. Sponge rubber and felt pads were cut to fit the areas on the chest wall which were to be compressed. The binder was applied so that the pads were most effectively pressed into these areas. It was used to encircle the lower chest just below the axillae, or to include one or both arms. To determine its efficiency, it was applied to six normal male medical students and to five patients who had just had thoracoplasties.* Measurements were made of the vital capacity, and the position and excursion of

*The experimental work was done with the help of Dr. Theodore Dasler and Dr. Sion Rogers. The orthopedic devices have been made by Mr. John Crawford and his associates in the orthopedic brace shop.

the diaphragm and chest wall during inspiration and expiration were noted by fluoroscopy (before and while the binder and pads were in place). It was found that the binder immobilized the hemithorax, forced the patient to rest, and only rarely modified the vital capacity. The disadvantages included a fixation of the contralateral wall, a lowering and increased excursion of the diaphragm, and a limitation of the patient's freedom. The method was used after thoracoplasty in twenty-eight cases during 1935-36, and was then discontinued.

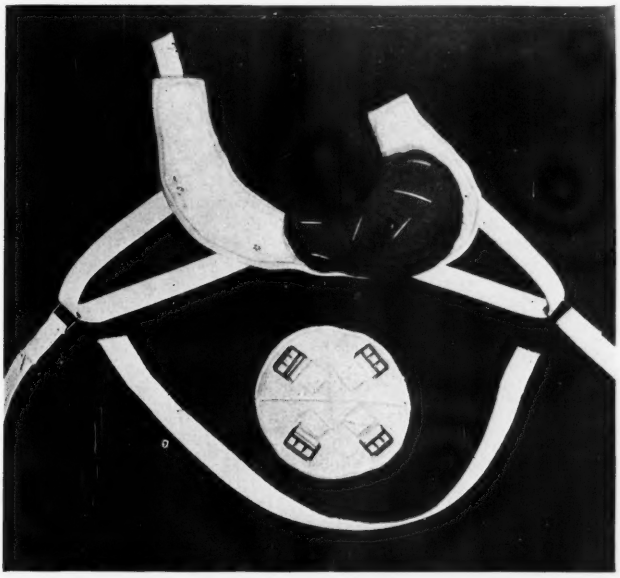

Fig. 3.—Underside of padded harness; hip pad.

The third device which has been tried is a padded leather harness. It is somewhat similar to the harnesses of Sauerbruch, Oelgoetz, and Woodruff, but adheres to principles which exclude encircling the chest and an excess of straps. It consists of a canvas pattern covered with lightweight leather which is shaped to encircle the shoulder and cover the anterolateral operated area. There is a buckle at the top of the shoulder; straps leading from the front and back to a pad with buckles at the contralateral hip; and a felt-padded perineal strap to fix the hip pad in position. Compression on the decostalized area is obtained by means of tailored pads sewn to the inner side of the anterolateral portion of the harness. In improving the efficiency, a belt was discarded as unnecessary; the front section was shortened; the use of sponge rubber has largely been replaced by a medium hard felt; and the straps are now riveted to the leather, rather than sewed, in order that pull on the straps may be directed more easily (Figs. 3 and 4).

The harness was at first used experimentally on a series of intact and post-thoracoplasty chests in the same manner as the binder. The effect was less easily demonstrable after operation than on the intact chest. It was found that the harness compressed and immobilized the upper chest wall, leaving the lower chest and arms unhampered. The vital capacity was not lowered, except in two cases in which the diaphragm failed to compensate. The shoulder was depressed by the harness, which not only corrected the tendency to elevation but decreased the use of accessory muscles in inspiration.

Fig. 4.—Harness, hip pad, and leg strap in place.

Clinically, the harness has been satisfactory. It has been used in ninety-eight cases in the past two years. All have had two or more posterior stages of thoracoplasty, and many, an additional anterior stage. A few days after the final operation in each case, a canvas pattern is cut to fit the individual patient and the position of the straps is marked by the physician. The pattern is then covered with a thin layer of leather; straps and buckles are added, and the hip pad and perineal strap are made by the technician. The harness is fitted on the patient, and the areas for compression of the anterior and axillary chest wall are marked. A laminated, tailored pad is then made from layers of felt and sewed in place. The patient then wears the harness for a few days, when it may be revised for a better fit. More pads can be added at later dates.

The cost of a harness can be as low as two or three dollars. It is quite rugged and lasts far beyond the four to six months of use. It can easily be worn from twenty to twenty-four hours a day after the first week.

Its major disadvantage is the need for an interested physician or technician to arrange a good fit. An understanding of effect and methods can best be obtained by wearing one.

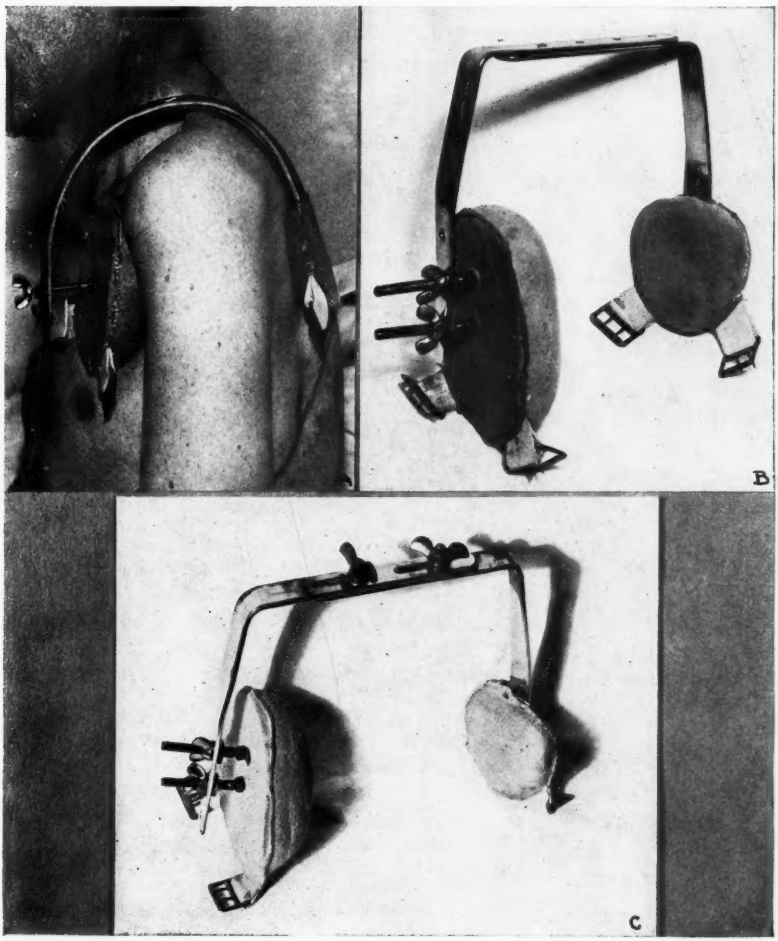

Fig. 5.—*A*, First spring brace; *B*, modified brace; *C*, brace with adjustable shoulder-piece.

Plastic weights have been used for compression and immobilization. The sandbag has been discarded for such purposes, and only the 3- to 8-pound shotbags are now used. They are applied to the anterior chest wall between stages, and on top of the harness after the last stage.

The fifth device which we have used is the brace described by John Steele. This is applied for anterior compression after an anterior or paravertebral first stage. It has been used in twenty-two cases.

The brace has been modified in several ways. The contralateral fixation has been changed from the axilla to the hip, although this is not important since it acts merely as a guy. Pressure by the original brace was obtained by means of the spring steel arc, but this needed repeated bending. In order to obtain better approximation of the front and back pads, an adjustable top section was devised which works very well (Fig. 5). Small felt pads are often placed under the anterior pad to obtain more intimate pressure. The chief limitations of the brace are discomfort and a resultant brief period of use. They are difficult to construct, but may be used on several cases before worn out.

NONSURGICAL CASES

We have had almost no chance to use orthopedic devices for nonsurgical tuberculosis. Abdominal binders have been applied in several cases with emphysema, but the presence of a pneumothorax on one or both sides has usually interfered with perfect usage. Binders, with pads or pneumatic bags beneath, have been used immediately post partum in four cases, but intolerance and complications have prevented a remarkable effect.

Shotbags have been applied to the anterior chest wall of a few nonsurgical patients, but a more promising method is the use of the lightly padded harness. It may be used on ambulatory or bed patients; it is well tolerated and produces an eventual flattening of the chest wall. One patient has worn such a harness at work for two years. The ideal indication would seem to be a unilateral lesion which has shown only a tendency to low-grade activity from the strain of increased shoulder or respiratory movement.

SUMMARY

There are apparently many good, simple mechanical aids to collapse therapy.

The sandbag, shotbag, pulley, brace, and harness have been found indicated and useful, and there is experimental and clinical evidence that they are efficient.

It has been said that they must be "applied with patience and care." Their theory and practice should be explained to the patient and a constancy of use repeatedly urged. The success of these methods rests almost entirely in the hands of the sanatorium physician.

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ANOMALIES OF THE LUNGS WITH SPECIAL REFERENCE TO THE DANGER OF ABNORMAL VESSELS IN LOBECTOMY

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THE recent advances in thoracic surgery, and especially the success of the operations of lobectomy and pneumonectomy, call for caution in the recognition of anomalies in the lungs and their vessels. Even so complete a source of information as Schwalbe's *Missbildungen des Menschen und Tiere*[1] is singularly incomplete as regards the anomalies of the vessels. Thoracic surgery has outgrown the laboratory, and our knowledge of the embryology, comparative anatomy, and physiology of the pulmonary and bronchial vascular systems during the last generation has not kept pace with it. The two classical experiments on the interdependence of the systemic and pulmonary vascular systems, those of Valsalva (1740)[2] and Johannes Müller (1838)[3] have disappeared from the existing textbooks of physiology, notwithstanding a serious effort by Crowden and Harris[4] to revive them, especially for routine use in the radiologic clinic.

H. M. Evans[5] and Thoma[6] by their individual researches have emphasized the importance of regarding the vascular system of the early embryo as a capillary plexus which grows in all directions. Subsequently certain channels in the primitive capillary plexus enlarge and give rise to the named arteries and veins of the older embryo, fetus, and postnatal forms. Many parts of the capillary plexus may persist or disappear, and it is the normal range of variation in these processes which accounts for most of the anomalies. The rigid adherence to the diagrams of the great arteries and aortic arches first published by Rathke (1825) and to the diagrams of the great veins and the cardinal system of veins, also published by Rathke (1830), has been responsible for the failure to recognize the diversity of patterns which may arise in either the arterial or the venous system.

Accessory pulmonary arteries and veins have been described in many vertebrates, ranging from amphibia and reptiles to mammals and man. Even as far back as 1837 Hyrtl[7] described accessory pulmonary arteries as a normal occurrence in snakes. He observed a series of pulmonary arteries arising from the dorsal aorta, which passed laterally to the posterior vesicular portion of the much elongated lung. Since the lungs and trachea are formed as an outgrowth from the primitive foregut,

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it is only natural that their actual substance should be supplied by ventral visceral branches of the dorsal aorta, in series with the coeliac axis and the superior mesenteric and inferior mesenteric arteries to the fore, mid, and hind gut. Quite apart from the definitive bronchial arteries, one to three in number for each lung, which arise from the aorta or from an upper intercostal artery, Turner[8] has described small branches of the intercostal arteries which pass to the pulmonary pleura and surface of the lung through the ligamentum latum pulmonis. These small arteries are constant.

ABNORMAL PULMONARY ARTERIES

McCotter[9] analyzed nine cases of abnormal pulmonary arteries. In seven cases the anomalous artery arose from the thoracic aorta; in one case, from the abdominal aorta, passing upwards through the esophageal hiatus in the diaphragm; and in the last case a large artery was given to the lung from an intercostal artery. In four of these cases the lobulation of the lungs was normal, and in five there was an accessory lobe of the infracardiac type. In the case in which the pulmonary artery arose from the abdominal aorta, branches were supplied to both lungs. In the five cases of abnormal pulmonary artery associated with atypical lobulation, four cases were left-sided and one right-sided. It is probable that the anomalous right bronchial artery running from the right subclavian artery to the lung in the case described by Menke[10] was functionally an abnormal pulmonary artery, as its diameter ranged from 5 to 6 mm. Batts[16] has recently published another case where a large pulmonary artery to the right lower lobe arose from the coeliac axis.

All the anomalous pulmonary arteries fall into two groups. The first group consists of persistent enlargements of embryonic capillary plexuses between the subclavian (fourth aortic arch), superior intercostals, or ventral splanchnic branches of the thoracic aorta on the one hand and the pulmonary artery proper (sixth aortic arch) on the other. The second group consists of persisting enlarged capillary plexuses between the abdominal aorta and coeliac axis on the one hand and the pulmonary artery on the other. In view of the frequency with which communicating branches are found between the coeliac axis and superior mesenteric artery, it is surprising that contributions from the abdominal aorta or coeliac axis to the lung do not occur more frequently. A cranial or caudal displacement of an artery of supply is common, as in the cases where the hepatic arteries arise in part or entirely from the superior mesenteric artery, or where the superior hemorrhoidal artery arises from the superior mesenteric artery.

ABNORMAL PULMONARY VEINS

The anomalies of the pulmonary veins are probably far more common than the recorded cases would suggest. The description of the

great veins in the chest by John Marshall (1859),[11] together with his account of the oblique vein as a remnant of the left superior vena cava of the embryo, has inhibited further research. The general principles enunciated by H. M. Evans and Thoma again clarify the position. The pulmonary and bronchial veins are the eventual persisting form of an originally vast indifferent plexus of capillaries in relation to the primitive foregut and its lung bed.

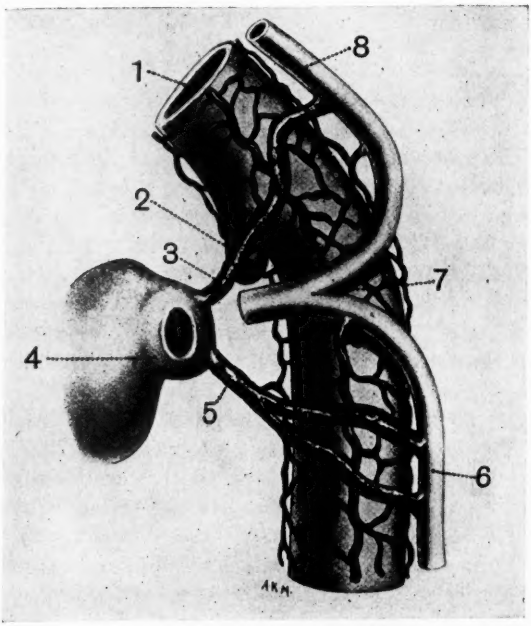

Fig. 1.—Reconstruction of a 4.5 mm. cat embryo (after A. J. Brown). *1*, foregut; *2*, lung bud; *3*, cephalic "tap"; *4*, sinus venosus; *5*, caudal "tap"; *6*, postcardinal vein; *7*, duct of Cuvier; *8*, anterior cardinal vein. The cephalic and caudal "taps" show how the future pulmonary veins and the future inferior vena cava anastomose via the gut plexus with the anterior and posterior cardinal veins. (From Harris, Gray, and Whitney: Anat. Rec. **36**: 31, 1927.)

The sinus venosus (and later the left auricle) receives two veins from the gut plexus, superior and inferior to the developing lung bud. The gut plexus in turn has numerous capillary anastomoses with the anterior and posterior cardinal veins (Fig. 1). The superior vein becomes the definitive common pulmonary vein; the inferior vein becomes the hepatic portion of the future inferior vena cava. At a later stage, with the development of the left auricle and the paired pulmonary veins, the anastomoses with the anterior or posterior cardinal vein may persist. Thus the venous anomalies in the adult will consist of one of two types. In the upper thorax will be seen persisting communications between the pulmonary veins and the derivatives of the anterior cardinal veins, communications with the superior vena cava,

innominate or jugular systems; in the lower thorax will be communications with the hepatic part of the inferior vena cava in the abdomen. The embryology of these venous communications was carefully studied by A. J. Brown,[12] and a case of a large vein running from the right internal jugular to the left (pulmonary) auricle in a child was described by Harris, Gray, and Whitney.[13]

BRONCHIAL ARTERIES AND VEINS

This important vascular system, closely related to the ramifications of the bronchi and associated with the nutrition of the lung substance and with the lymphatic glands and nodes of the bronchial tree, still awaits elucidation. Little has been added to the description in *Quain's Anatomy.*[14] Nakamura[15] has analyzed 150 cases as to the actual site of origin of the bronchial arteries, from the aorta or intercostals; the number ranged from one to three in each lung.

The bronchial veins are not so extensive in their distribution as the bronchial arteries. They are said to drain both peripherally and centrally and, to some extent, directly into the pulmonary veins. Veins from the larger bronchi and from the lymphatic glands are also said to drain directly into the pulmonary veins rather than the bronchial veins, which usually terminate in the vena azygos major on the right and the superior hemiazygos on the left.

Little is known of the comparative anatomy and embryology of the bronchial arteries, veins, and lymphatics. The extent and nature of the anastomoses on the venous side between the pulmonary and bronchial veins may be of some significance in relation to thrombosis and embolism. Broadly speaking, the development of the bronchial arterial system is roughly proportional to the development of the lymphatic vessels and glands in the chest. This is well seen in the lungs of the ox where, even to the naked eye, the individual lung lobules seem to be floating in a lymph sac. In this form, pneumonia displays a rapid crowding of the lymph spaces with fibrin and leucocytes, as distinct from pneumonia in man where the exudate is essentially intra-alveolar.

REPORT OF CASE

The patient, a girl aged 5 years, was transferred to the North Middlesex County Hospital from an isolation hospital on March 7, 1936. She had been in the fever hospital for seven weeks with scarlet fever, developing "bronchopneumonia" and coughing up a quantity of pus a week before transfer. On admission to the North Middlesex she was found to have an abscess in the upper part of the left lower lobe. On March 9, 1936, operation for drainage was performed, but as the pleural adhesions were not very dense, the wound was packed and the abscess itself opened a week later. The cavity was the size of an orange. Hemolytic streptococci were cultivated. After the operation the toxemia and fever rapidly subsided. The cavity diminished, but a lipiodol x-ray on May 11 showed bronchial fistulas and extensive associated bronchiectasis secondary to the abscess. During the summer she gained several pounds in weight and the wound healed over, although she still coughed up pus and the sound over her left lower lobe was dull.

On Sept. 28 large portions of the eighth and ninth ribs were resected, and the cavity in the lung was reopened and packed. The patient's general condition improved, but, owing to healing of the chest wall, another de-roofing operation was carried out on Dec. 3, 1936, and it was again packed wide open. The appearance now was typical "lattice-lung." It became evident that the condition could no longer be cured without dealing with the bronchiectasis which had supervened, but a lobectomy in the presence of so much suppuration in the chest wall was not to be considered lightly. Therefore, in order to reduce the sepsis and secure a clean granulating cavity, on Feb. 17, 1937, a great part of the sixth, seventh, eighth, and ninth ribs was removed, together with the intercostal bundles and the roof of the cavity. As a result, a clean granulating cavity was produced, with the bronchiectasis persisting as before. As the patient's condition was now considerably improved and the condition of the chest wall cleaner, it was decided to carry out lobectomy. This was undertaken on May 4, 1937, under cyclopropane anesthesia. The usual posterolateral incision was made, through the old scar. The pleura was still free over the upper lobe and much disturbance was caused on opening it. The lower lobe was densely adherent to the chest wall, mediastinum, and diaphragm.

Fig. 2.—Posterior view of thoracic organs of E. D., aged 5 years. A pencil has been passed into a large anomalous pulmonary artery arising from the thoracic aorta 2 cm. above the diaphragm. This point is seen to be at the level of the free margin of the pulmonary ligament in the opposite lung.

The worst area of all, however, was in the paravertebral groove, where the adhesions were extremely dense and continuous. These were being freed little by little, alternately wiping with gauze and cutting with scissors. Eventually, when the bodies of the vertebrae were reached, the lung had to be separated in the extrapleural plane. Near the end of this stage a strand of tissue was snipped with scissors; there was violent and profuse arterial hemorrhage. This was controlled by the finger; its precise origin could not be made out owing to the adhesions and blood, but the aorta could be felt directly underneath. It was controlled by a firm pack sutured in position. As the condition of the patient was very bad, the

operation was abandoned, the patient returned to the ward, and a blood transfusion begun. Despite all measures, however, she died one and one-half hours later.

At the post-mortem examination it was found that a large abnormal artery arising from the aorta had been snipped partly across, 0.5 cm. from its origin. The artery arose from the descending thoracic aorta 2 cm. above the diaphragm, passing into the left lower lobe of the lung at a level corresponding to the free margin of the pulmonary ligament (but this structure had disappeared in the dense adhesions). The artery was as large as the patient's coeliac axis (Fig. 2). The aorta was undamaged.

SUMMARY

1. A fatality due to damage to a large abnormal pulmonary artery during lobectomy is reported.

2. This artery, of the same diameter as the coeliac axis, arose from the descending thoracic aorta 2 cm. above the diaphragm and entered the posterior border of the left lower lobe.

3. Its occurrence has suggested the need for careful recording of all anomalies in the chest, as well as for much intensive research on the embryology and comparative anatomy of the pulmonary and bronchial vascular and lymphatic systems.

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FIBROMA OF THE ESOPHAGUS

Report of a Case

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In 1933, Patterson,[1, 2] in an article entitled "Benign Tumors of the Esophagus," stated that, after a careful search of the literature, she had been able to collect records of sixty-two cases published between the years of 1717 and 1932. Since this time a number of isolated cases have been described, and the condition is no longer a pathologic curiosity. It is true that no individual surgeon has been able to gain personal experience of a large series of cases; but it is well for those interested in thoracic surgery to be familiar with the facts, and, consequently, it may be useful to summarize the recorded features of these tumors.

The following are the chief pathologic types which have been described: adenoma, aberrant thyroid tumors, cysts, fibroma, hemangioma, leiomyoma, lipoma, lipomyoma, myxofibroma, neurofibroma, papilloma, and polyp. It seems unlikely that any of these become malignant, but degenerative processes such as calcification are not uncommon and may lead to confusion in interpreting x-rays. In the experience of Moersch and Broders,[3] the commonest clinical types are polyp, myoma, and papilloma, and the latter are frequently multiple.

In 1926, Vinson, at the Mayo Clinic, estimated that benign tumors were present in only three cases in a series of approximately 4,000 patients who complained of dysphagia. This figure gives an inaccurate impression of the general incidence, for it is well known that a high proportion cause no symptoms and many of the cases which have been described were first discovered at autopsy.

Benign tumors are said to show a preference for the upper and lower ends of the esophagus, but they may arise from any part.

As far as clinical types are concerned, it is convenient to consider two groups, namely, those which arise in the mucosa or the submucosa, and those which grow from the outer coats. The former, which comprise the majority, are sessile or pedunculated. When examined with an esophagoscope, the sessile tumors are firm, smooth, or nodular, and are covered with normal epithelium; they rarely attain sufficient size to cause symptoms, but bleeding does occur and is either the result of ulceration due to trauma, or to the presence of an hemangioma. These are the cases which form the bulk of the material discovered unex-

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pectedly at autopsy. In rare instances, sessile tumors grow larger; the sequence of events then resembles that found in other parts of the alimentary tract where peristaltic waves grip the mass and try to pass it onward. Varying degrees of intussusception, associated with hypertrophy of the muscle tissue in the walls of the adjacent gut or with the formation of a diverticulum,[4] can occur, and these patients complain of dysphagia and regurgitation of food.

When a tumor becomes pedunculated, the progress and possibilities are different. The pedicle is apt to grow to a great length so that the tumor hangs upon a stalk. In such a case, the patient may be surprised and mystified by the appearance in the mouth of an oysterlike mass, which vanishes as suddenly as it comes, during spasms of retching; there may be no other symptoms, but instances are on record of patients in whom, during sleep or coughing, the tumor has become impacted in the larynx and caused death from suffocation. Chitty[5] and others have described pedunculated tumors which protruded permanently several inches beyond the teeth, and which had the appearance of an enormous tongue. Growths of this type should be removed, and the operation has been successfully performed through the mouth and also by exposing the esophagus in the neck or mediastinum and dealing with the pedicle in this way. It is unwise to avulse the tumor because bleeding may occur and because more thorough treatment of the pedicle is necessary to prevent recurrence; it is also unsound to delay operation in the hope that the patient may expel the mass during an attack of vomiting, although this has been recorded.

The second and more rare group of cases is that in which the growth has its origin in the tissue outside the mucosa. These tumors grow slowly and steadily and are more likely to extend outward than to occlude the lumen. As the mass increases in size, the mucosa is stretched upon the surface of the tumor and the actual lumen of the esophagus is increased rather than diminished. If the growth encircles the gut, however, obstruction may be produced ultimately. The lesion is frequently silent until it has reached such a size as to cause mediastinal obstruction, a factor which is more important in the superior mediastinum than elsewhere because the available space is less in this part. The great veins and the trachea are compressed first, and J. Meyer has described an advanced case in which the left recurrent laryngeal nerve was also paralyzed. Pain behind the sternum and a troublesome cough are features of some cases.

The claims, which have been advanced, that a diagnosis can always be made radiologically are probably unsound; it is not even true that all types of benign tumor can be diagnosed by esophagoscopy, unless it is considered safe to pass an aspirating needle through the mucosa or to make an incision and obtain a small piece of tissue for section and microscopy.

The tumor described in this report is a fibroma of unusual size. It is interesting because the patient was admitted as a case of bronchial obstruction complicated by secondary changes in the lungs. The signs and symptoms did not suggest an abnormality of the esophagus, and the true diagnosis was not known certainly until after operation. The tumor could not be shelled out from the esophageal wall because the muscle coats were so thin and atrophied that the mucosa would have been left unsupported over a large area; to cure this patient it would have been necessary to resect a great part of the esophagus.

The patient died after the operation and her death was due to the operative procedure and to a serious aggravation of the bronchial obstruction; at no time was there any difficulty in swallowing. It would have been possible to mobilize the esophagus and, having divided and invaginated the lower end, to bring the upper part, including the tumor, out upon the surface of the neck, but circumstances peculiar to this case—age, mental state, and so forth—made it preferable, in our judgment, to leave matters as they stood.

It is difficult before operation to know whether it will be possible to enucleate such a tumor without important injury to the esophagus, and although Edward Churchill[6] has described a case in which he succeeded in shelling out a smaller growth with complete success, it appears that in cases similar to the one reported here the choice lies between palliative treatment on the one hand and esophagectomy on the other.

CASE REPORT

History.—Mrs. D. B., aged 66 years, was admitted to hospital complaining of cough, dyspnea, and "wheezing" in the chest. She was a normally developed woman and looked younger than her age. Her past history was rather indefinite, but she had been in an institution for mental disorders a few years before admission and had been subject to attacks of severe depression ever since. Nine months before admission she caught a "cold" and went to bed with pains in the chest, a temperature of 103° F., general malaise, and insomnia. In a month she slowly recovered and resumed her duties in the house. From this time onward, she was always troubled with dyspnea which was constant and which gradually became worse; six months, and again six weeks before admission she consulted her physician because of illnesses which were diagnosed as pneumonia. An x-ray of the chest was taken ultimately, and in this an abnormal shadow was seen in the superior mediastinum. She had lost no weight, and there was no disturbance of appetite or swallowing.

State on Admission.—The patient was a silent and depressed woman who sat up in bed because respiration was easiest in this position. There was some stridor and moderate dyspnea. She complained of an irritating and unproductive cough. The temperature and pulse and respiratory rates were normal. The thyroid gland was not enlarged, and there was no evidence to suggest a retrosternal goiter. There was an enlarged lymph gland in the supraclavicular space on the right side; a section made from this showed chronic lymphadenitis. The larynx was normal. In the chest the physical signs were those of a mass in the superior mediastinum causing no obstruction to the venous return but displacing the trachea far forward so that it appeared to lie subcutaneously in the suprasternal notch. There were crepitations over both lung fields.

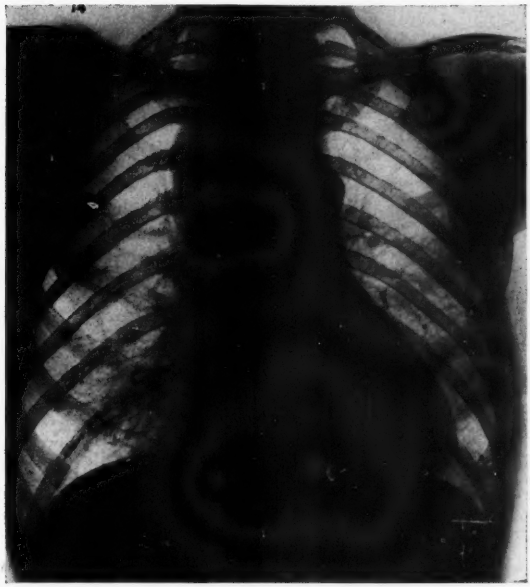

Fig. 1.—Anteroposterior view of the thorax showing the enlargement of the mediastinal shadow to the right above the aortic arch.

Fig. 2.—Lateral roentgenogram showing the anterior displacement of the trachea in the thorax.

Fig. 3.—Lateral roentgenogram taken after a barium swallow. Most of the emulsion has passed into the stomach, but the tumor is partially outlined and its close relation to the trachea can be seen.

Fig. 4.—Photograph showing the esophagus which has been opened from behind. The tumor occupies the upper part and protrudes into the lumen.

The cardiovascular system was normal for a woman of this age, and the blood tests for syphilis were negative. On this account, the possibility of an aneurysm was dismissed. There were no physical signs in the abdomen or elsewhere. The sputum was negative for malignant cells (Dudgeon's method) and for tubercle bacilli.

X-Rays.—The anteroposterior film showed a rounded opacity lying to the right of the aortic arch and stretching upward to the base of the neck (Fig. 1). The mass was about the size of a large apple; it was smooth in contour and without pulsation. In the lateral view, the shadow of the trachea was clearly seen and was arched over the front of the mass (Fig. 2). A barium swallow proved the shadow to be connected with the esophagus which was displaced to the right over a distance of about 4 inches, and although there was a slight holdup in the flow of the emulsion, most of it passed quickly into the stomach (Fig. 3). In the area occupied by the mass, the contour of the esophagus was abnormal and had the appearance of being eaten away.

Fig. 5.—Photograph of the tumor from the front. The trachea is seen to be flattened as it passes over the mass, which stretches from just below the larynx to the bifurcation. The trachea has been laid open.

These films were interpreted by some as diagnostic of a tumor in the wall of the esophagus and by others as suggestive of a mediastinal dermoid. A piece of tissue for microscopic examination was not obtained by endoscopy because it was considered dangerous to perforate the mucosa.

Although the exact diagnosis was uncertain, the patient's discomfort seemed to justify exploration of the tumor, in the hope that it might be possible to enucleate it from the mediastinum.

Operation.—Right anterior thoracotomy was performed with Dr. Magill as anesthetist. The larynx was cocainized and a tube passed into the trachea, but a satisfactory airway could not be obtained owing to the shape and length of the obstruction. An intravenous injection of pentothal sodium was given and this was followed by cyclopropane and oxygen.

The mediastinum was exposed across the right pleural cavity in the usual way, and the tumor was seen to form part of the wall of the esophagus. At first it seemed as though it might shell out quite easily, but after a brief trial, the effort was abandoned when it was realized that this could not be accomplished without irreparable damage to the esophagus. The proposition of esophagectomy was then considered but not attempted on account of the patient's age and unsatisfactory mental state.

The mediastinal and parietal pleura were repaired, and the chest was closed without drainage.

Postoperative Course.—Death occurred thirty-six hours after operation. Respiratory distress and dyspnea were aggravated by the operation, and surgical emphysema appeared upon the neck and chest.

Autopsy.—There were no abnormal findings apart from those in the chest. The tumor was growing from the wall of the esophagus and measured 4½ inches along the gut and 2½ inches across (Fig. 4). In appearance it resembled the benign tumors of the same type which occur not infrequently in the wall of the stomach. The consistency was firm, the color grayish-white, and the contour smooth. The mucous membrane was intact except in one small area where it had been damaged at operation. The muscle coats were atrophied and, in the vicinity of the tumor, could not be identified. There were no pathologic adhesions to adjacent structures and no evidence of septic mediastinitis. The trachea was stretched and flattened over the front of the mass (Fig. 5), and the lungs showed bronchitis and emphysema.

Microscopy sections were diagnosed as fibroma.

SUMMARY

A brief description of the features of benign tumors of the esophagus is given.

The signs, symptoms, and treatment of a patient suffering from the effects of a large fibroma are described.

It is hoped that the description given may help others who meet such a case to make an accurate preoperative diagnosis and to achieve a successful surgical result.

EDITOR'S NOTE: Because the author is in active military service, it was impossible for him to correct the proof of his article.

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DIFFUSE POLYPOID LARYNGOTRACHEOBRONCHITIS

With a Preliminary Note on Endoscopic Curettage

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OBSTRUCTING bronchial tissue may be malignant, benign, or inflammatory. Of the first group, much has been written. In the second group, adenomas apparently are the most common and are attracting increased attention.[1] Other less common benign tumors have been described by Jackson and Jackson.[2] The various types of "inflammatory tumors" are not well understood. Contributions by Jackson and Jackson, Peroni,[3] and Pollak and his co-workers[4] give a good summary of the literature.

The following case of diffuse inflammatory tracheobronchial obstruction is of sufficient rarity and interest to warrant a report.

F. S., a white male, aged 71 years, was referred to the Alameda County Cancer Clinic by Dr. Theodore Lawson. He had been well until eight years previously. His first symptom was cough, which, at first, was only occasional and nonproductive. Within two years the cough increased in severity until it was present at all times. It was characterized by wracking paroxysms lasting many minutes. At this time the cough became productive, and the patient raised from 100 to 150 c.c. of sputum in twenty-four hours. It was purulent and occasionally had a musty odor. There were no hemoptyses, but on two occasions there was streaking over a period of several days. These were nine months and five weeks prior to admission. Shortly after the development of cough, a slowly progressive hoarseness appeared. On admission the patient could not speak above a whisper. There was a gradual weight loss of from 210 to 126 pounds. For about three years before admission there had been moderate dyspnea on exertion. There was no orthopnea.

The patient had worked in cement as a hoisting engineer for thirty years. The past and family histories were irrelevant. There was no known contact with tuberculosis.

The physical examination showed an elderly, poorly nourished male. He was extremely hoarse, he coughed frequently, and there was a definite stridorous wheeze associated with an obstructive type of breathing. Slight dyspnea was present. The hearing was diminished bilaterally and there was slight loss of visual acuity. Inside the right cheek was a papillomatous, whitish mass (subsequent microscopic examination showed hyperkeratosis). The lungs showed dullness over the right upper lobe. Tnere were increased breath sounds and a few fine râles. The heart was normal in size and the rhythm was regular. Blood pressure was 100/60. There was evidence of generalized arteriosclerosis. The liver extended 4 cm. below the right costal margin. There was a small left inguinal hernia which was easily reducible. The rectal examination showed a slightly enlarged prostate, and internal and external hemorrhoids were present.

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The essential laboratory findings were as follows: The urine showed a trace of albumin and from thirty-five to forty white blood cells per high dry field. The blood showed hemoglobin, 88 per cent; red blood cells, 4,690,000; white blood cells, 7,700, with a normal differential. The Wassermann reaction was negative; the sedimentation rate (Cutler) was 20 mm. in one hour. Many sputum examinations, including a guinea pig inoculation, showed absence of acid-fast bacilli. A sputum culture showed a few yeastlike fungi. The intradermal tuberculin test was negative (0.1 mg. O.T.). Vital capacity was 2,100 c.c. A posteroanterior thoracic roentgenogram (Fig. 1) showed depressed diaphragms bilaterally, with basal emphysema. The trachea and upper mediastinum were retracted to the right. Nodular densities were present at the right hilum. The right upper lobe was greatly fibrosed and shrunken. There were multiple, small, rounded areas of decreased radiolucency, in at least one of which was a fluid level. This was confirmed fluoroscopically. The areas were suggestive of bronchial dilatation. The heart was normal in size and the left lung was entirely clear.

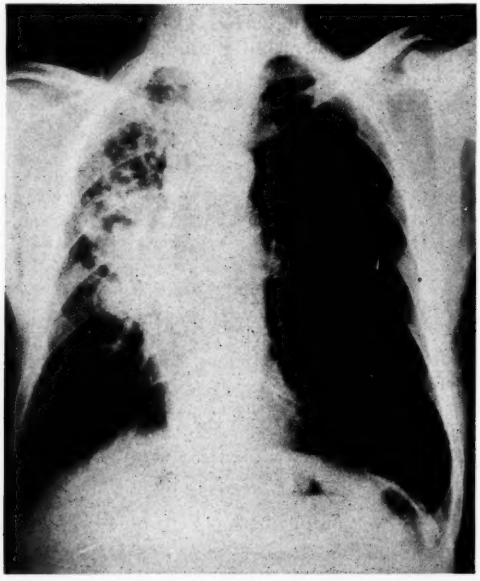
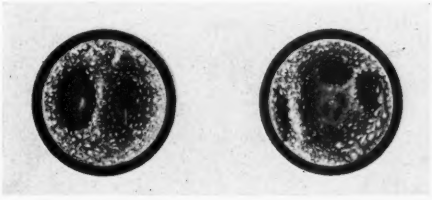


Fig. 1.—Posteroanterior thoracic roentgenogram. (See text.)

A thoracic roentgenogram had been taken six years previously, and at that time the patient was told that he had an extensive chronic infection in his right lung. Numerous sputum examinations performed elsewhere had failed to reveal acid-fast bacilli.

An immediate bronchoscopic examination was recommended by the cancer clinic. Ten per cent cocaine was applied locally. Mirror laryngoscopy showed that the posterior surface of the epiglottis was irregular from the heaping up of a soft reddish-yellow tissue. The anterior commissure was infiltrated, but the cords themselves were not involved and there was no paralysis. The ventricular bands were moderately swollen and nodular. The posterior arytenoids were normal. The 8 mm. 40 cm. Jackson bronchoscope was passed with care. No normal tracheal mucosa was visible. The surface was covered with discrete and confluent masses of reddish-yellow polypoid tissue which were slightly elevated above the surface.

The greatest change was on the anterior and right anterolateral wall of the trachea. The tissue was very friable and showed definite to-and-fro motion on cough. The involvement was more extensive in the lower trachea. At the carina (Fig. 2*A*) the masses were completely confluent and involved the right stem bronchial orifice to a much greater degree than the left. Tenacious purulent secretions were coming from the right side. There was no fibroid stenosis and both main bronchi could be entered with the bronchoscope. The right upper and middle lobar orifices were identified, but were almost completely occluded (Fig. 2*B*). Purulent material oozed from the upper lobar orifice. The mucosal change was less extensive in the right lower lobe and throughout the left stem bronchus, but no normal mucosa was seen. Following the use of a scalping motion with the bronchoscope, many pieces of tissue were coughed out. In this manner an attempt was made partially to open the occluded bronchi.



A. *B.*

Fig. 2.—*A*, Bronchoscopic view of carina showing complete loss of normal mucosal pattern. The right stem bronchial orifice is partially occluded by small, friable, polypoid masses.

B, The lip of the bronchoscope has been maneuvered through the tissue obstructing the right main bronchus. The upper and middle lobar orifices are almost completely occluded. Purulent secretions ooze from the upper lobe opening on cough.

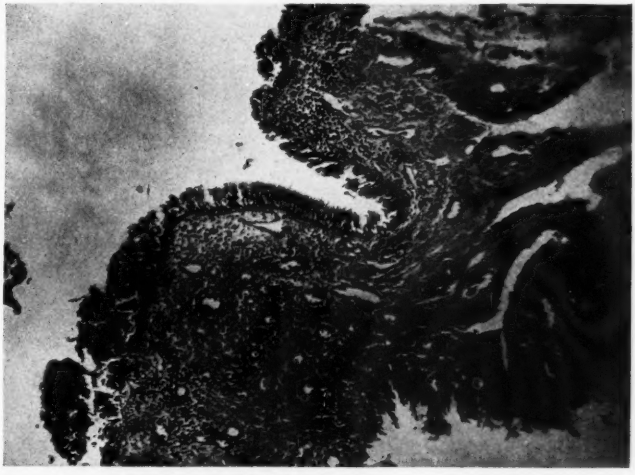


Fig. 3.—Photomicrograph of typical polyp secured at biopsy (×300). There is no epithelial metaplasia. There is much inflammation in the hyalinized submucosal tissues.

Numerous biopsy specimens also were procured at various levels.

The pathologic report was made by Dr. Gertrude Moore: "Diffuse polypoid hyperplasia of the tracheal and bronchial mucosa, showing both acute and chronic inflammation." (Fig. 3.)

Following bronchoscopy there was improvement in cough, but the patient left the hospital against advice before further treatment could be given. Five months later he died in an ambulance on the way to the County Hospital. No detailed history could be obtained, but it was reported that he had suffered increasing disability from dyspnea, cough, and aphonia during this interval. A limited autopsy showed that the immediate cause of death was bilateral bronchopneumonia and terminal cardiac dilatation.

The sternum and cartilages were removed. The left lung extended past the midline to the right sternal margin. The lungs, heart, trachea, and larynx were excised en masse.

The *heart* was approximately the normal size; the walls were flabby. The valve cusps were normal, and the tricuspid valve admitted five fingers, with ease. A chicken fat clot was present in the right ventricle. The aorta showed advanced atherosclerosis with calcification.

The *left lung* was greatly increased in volume. The upper lobe was emphysematous; the lower lobe was boggy, extremely congested, and the site of early confluent lobular pneumonia.

The upper and middle lobes of the *right lung* were contracted and airless. There was extensive fibrosis; multiple bronchial dilatations of various diameters were seen. In some of these the walls were completely destroyed (bronchiectatic abscesses), and the lower lobe was emphysematous. The edema, congestion, hemorrhage, and diffuse confluent lobular pneumonia were more advanced than on the left side.

Fig. 4.—Photograph of larynx, trachea, and upper portions of stem bronchi. The ventricular bands are greatly enlarged. The right stem bronchus is above. There is nearly complete occlusion of the right upper lobar bronchus.

Trachea and Large Bronchi (Fig. 4).—The lower airway was opened from behind, and the posterior surface of the epiglottis was roughened. The ventricular folds bulged into the lumen and almost touched in the midline. There was no gross ulceration, but it could not be determined whether epithelium covered these masses. The entire trachea was infiltrated with a tissue which was golden-yellow in color. The surface was smooth in some areas and roughened in others. Where rough, the tissue was friable and could be removed by scraping with a blunt instrument. Minute polypoid projections could be made out everywhere. The most extensive change

was in the lower trachea. The lumen of the right stem bronchus was at least three-fourths diminished. The right upper and middle lobar orifices were entirely occluded by projecting tissue. There was diffuse, flattened infiltration throughout the lower lobe bronchus. Dissection of the third and fourth order bronchi disclosed a minute surrounding ring of yellowish tissue which partially occluded the lumen. On the left the condition was entirely similar, except that it was not so advanced. No orifices were entirely occluded, although the condition extended well into the smaller bronchi.

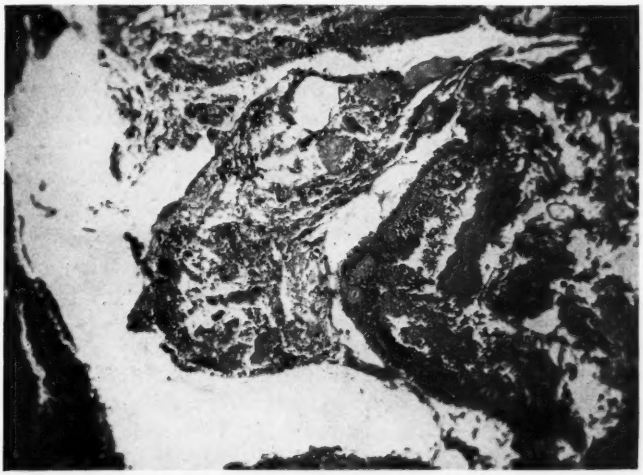


Fig. 5.—Photomicrograph of 3 mm. bronchus (×100). The bronchial wall is at the left and below. At the right and above, two polypoid masses protrude into the lumen. The surface epithelium is desquamated, and there is extensive submucosal hyalinization. The bronchial lumen is reduced further by the mass of fibrin and leucocytes which is seen in the center of the illustration.

The microscopic sections were studied by Dr. Louis H. Dyke, Jr.: "There is partial desquamation of the surface epithelium which, however, retains its stratified, ciliated, columnar characteristics. The basement membrane is widened. A typical polyp shows extensive submucosal hyalinization with diffuse chronic inflammatory infiltrations. Sections taken from the relatively smooth areas in the trachea show fewer polypi. In these regions the mucosa tends to be thrown into wide folds. In general, the submucous glands are partially destroyed and surrounded with hyalin material which extends down to the cartilage. Many of the glands are the site of focal inflammatory infiltrations." (See Fig. 5.)

COMMENT

This case is unique because of the extent of the tracheobronchial pathology. In Pollak's collected series, all "inflammatory polyps" were single and no cases of diffuse polyposis were reported. Unfortunately, the patient left the hospital before bronchograms could be made. The description of the bronchogram in Beutel's case[5] is similar to what one might have expected here. The pathologic report in Beutel's patient was, however, multiple papillomas. These were apparently secondary implantations from a laryngeal papilloma.

In a discussion of possible etiology, it appears to make little difference whether the mucosal hyperplasia is localized, i.e., a single "inflammatory polyp," or whether it is widespread, i.e., diffuse polypoid tracheobronchitis or polyposis. The cause of polypoid mucosal change is still a moot question. The Jacksons[2] feel that it probably *follows* pulmonary suppuration and is due to the constant irritating action of purulent sputum on the mucosa. Peroni[3] was of the belief that bronchial polyps undoubtedly were inflammatory in origin. He felt, however, that the inflammation was primarily bronchial, and that the various types of pulmonary suppuration were secondary to bronchial obstruction. Peroni was unable to reproduce these lesions in dogs by infecting or irritating either the bronchi or the lungs. This cannot be used as evidence since dogs are notoriously resistant to infections of this type.

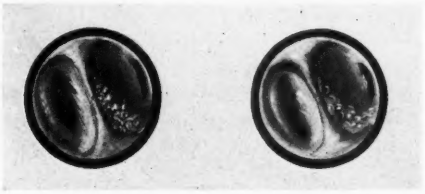
Peroni further expressed the belief that, if inflammatory hyperplasia were secondary to pulmonary suppuration, they should be seen more often in cases of bronchiectasis and chronic pulmonary suppuration. The writer feels that this may be, in a large measure, due to individual susceptibility of the mucosa. In a few persons there is an abnormal tissue reaction to relatively minor forms of irritation. By analogy to the upper respiratory tract, inflammatory nasal polyps do not occur frequently in cases of chronic sinusitis. Usually we do not procure mucosal biopsies in cases of pulmonary suppuration unless a definite tumescence is present. Because of this, it is probable that many early cases of inflammatory mucosal hyperplasia are missed. Studies are being undertaken at the present time to confirm this supposition.

A review of the case reported above supports the belief that the polypoid mucosal hyperplasia was secondary to bronchiectasis and pulmonary suppuration. Roentgenograms taken shortly after the patient became ill showed extensive infection in the right lung. By the time death had supervened, there was diffuse polyposis, but it was much more extensive in the bronchi draining the bronchiectatic lobes and less marked in the upper portions of the trachea. This corresponds in all particulars with the spread of an extensive tuberculous tracheobronchitis, which is generally agreed to be secondary to pulmonary tuberculosis. The laryngeal involvement was apparently progressive, since there was considerably more disease of the ventricular folds at the time of death than at the time of bronchoscopy, five months before.

The following case was reported in detail elsewhere.[6] It offers important confirmatory evidence as to the secondary nature of polypoid mucosal hyperplasia.

A man of 34 years had a chronic suppurative pneumonitis of the right upper lobe. At bronchoscopy, large quantities of purulent sputum were being ejected with force from the right upper lobar orifice. On the mesial wall of the stem bronchus directly opposite this orifice was an irregular flattened tumescence (Fig. 6). Polypoid hyperplasia, granulation tissue, and neoplasm were considered. Two

small biopsy specimens were taken. Bronchoscopy resulted in marked clinical and roentgenologic improvement. Two weeks later a second endoscopic aspiration was done. The lesion had become flattened and more nearly resembled normal mucosa. Hyperplasia and edema were greatly diminished. The pathologic report was made by Dr. Gertrude Moore: "Polypoid bronchial mucous membrane showing chronic purulent inflammation. The submucosal stroma exhibits increased vascularity and early fibrosis. There is no evidence of epithelial metaplasia." (Fig. 7.)



A. *B.*

Fig. 6.—*A*, Bronchoscopic view showing a mass of polypoid mucosa on the mesial wall of the right stem bronchus directly opposite the upper lobar orifice.
B, Two weeks later. The lesion has flattened and the polypoid hyperplasia has diminished.
(Reprinted from Am. Rev. Tuberc. 38: 688-702, 1938.)

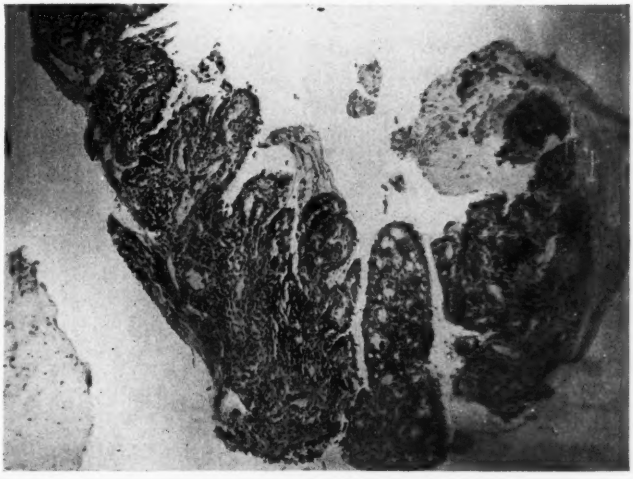


Fig. 7.—Photomicrograph of biopsy specimen (×200). (See text.)

This lesion developed in an area which was constantly bathed and traumatized by irritating secretions. It was sessile and, because of its position, could cause no conceivable obstruction either to the stem bronchus or to the upper lobar orifice. It is, therefore, only fair to assume that the inflammatory hyperplasia was entirely secondary to the pulmonary suppuration. The observed regression of the hyperplasia

coincident with improvement in the pulmonary infection is further substantiation of its secondary nature.

A comparison of the microscopic pathology in these two cases shows that the process is essentially the same in both, although of much longer standing in the case of F. S. In this patient extensive submucosal hyalinization occurred in what earlier was probably fibrovascular stroma. The similarity to the second patient thus is understood. The total absence of mucosal metaplasia in both cases is interesting, but it cannot be explained satisfactorily at the present time.

ENDOSCOPIC CURETTAGE

At the time when F. S. was examined bronchoscopically, no adequate means were available for rapidly removing obstructing tissue. Forceps were hopelessly inadequate because the polyposis was so widespread. In order to be prepared for a similar situation, special endoscopic curettes were designed (Fig. 8).* The shafts are of ⅛-inch stainless steel. The smallest curette illustrated can be used through a 5 mm. full-lumen Jackson bronchoscope. It may also be passed deeply into the tertiary lower lobe bronchi of an adult.

Fig. 8.

Fig. 9.

Fig. 8.—Three types of curettes which have been used. The shafts are of ⅛-inch stainless steel and are 44 cm. in length. The shape and size of the cups may be varied to meet special needs. The middle curette may be used through a 5-mm. full-lumen Jackson bronchoscope. (Reprinted from West. J. Surg. 49: 687-691, 1939.)

Fig. 9.—Special silver nitrate applicator with sponge. The sponge is held firmly by four prongs. The lower two prongs are on a flattened movable shaft which is raised and held in position by the threaded collar. A 7-cm. strip of "nu-gauze" with selvage edges is used for the sponge. The gauze is fashioned into a fairly loose roll, tied once through the midportion, and once halfway to the end which is held by the prongs. The gauze roll then is tapped gently to spread and flatten the applicator surface. (Reprinted from West. J. Surg. 49: 687-691, 1939.)

These instruments have been found of value in many instances. They have been used in approximately fifty cases without untoward results. Indications have been both for biopsy purposes and for treatment.

*These instruments were made by Mr. George Becker, Multi-Arc Laboratories, 4026 Grove Street, Oakland, Calif.

Experience in gauging side pressure is necessary in order that the bronchial wall is not penetrated. There appears to be a relatively wide margin of safety because the long shaft permits a moderate spring. Oozing has been controlled readily by packing and by cauterization. This has been accomplished by means of either the special silver nitrate applicator (Fig. 9)* or the high frequency unit.

After detachment of tissue, the curette is turned with the sharp edge upward. The tissue thus is held in the cup while the curette is being withdrawn from the bronchoscope. The tissue is removed from the curette by rapid agitation in a specimen glass containing normal saline solution. The specimen is sent immediately to the laboratory where the fluid is centrifuged. The sediment is then fixed in 10 per cent formalin, dehydrated, and blocked in paraffin in the usual manner.

To date, the curettes have been used in three main types of cases. In the treatment of tuberculous granuloulcerative lesions of the lower airway, removal of excess tissue by curettage has been accomplished prior to cauterization. At times, patients with bronchiogenic carcinoma have a diffuse infiltration of the bronchial wall and there is no projecting area from which a forceps specimen can be taken. In several of these cases, a positive diagnosis has been made from a study of the bronchial curettings. Relatively few cells may be obtained. This potential drawback is overcome by good pathologic consultation. The difficulty of securing adequate forceps specimens from sessile lesions is well known, and often the tissue is distorted. Curettage specimens may be obtained more readily from lesions of this type and usually have not been as crushed as those which were procured with the forceps.

As a special line of investigation, superficial mucosal biopsies now are being taken with the curette in selected cases of chronic bronchopulmonary suppuration. By this means it is hoped that some knowledge may be gained concerning early mucosal change, either in the direction of inflammatory hyperplasia or even of early tumor formation.

SUMMARY AND CONCLUSIONS

An unique case of diffuse polypoid laryngotracheobronchitis has been presented. The great diagnostic value of bronchoscopic examinations in thoracic disease again is brought out. The Jacksons feel that polypoid mucosal hyperplasia probably is *secondary* to pulmonary infection and is directly due to the irritating action of purulent sputum. Following a study of the two cases reported above, evidence has been presented which tends to support this view.

A preliminary note on endoscopic curettage has been given, based on experience in approximately fifty cases. It is believed that this technique may have both diagnostic and therapeutic value in selected cases. Endobronchial curettes are suggested as an addition to the armamentarium of the bronchoscopist.

*See footnote, p. 686.

The writer is grateful to Dr. Gertrude Moore, Consulting Pathologist, and to Dr. Louis H. Dyke, Jr., Resident in Pathology, Alameda County Institutions, for their aid in the preparation of this paper.

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411 THIRTIETH STREET

SITUS INVERSUS, SINUSITIS, AND BRONCHIECTASIS

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IN 1937 Adams and Churchill reviewed the literature concerning patients having complete transposition of the viscera, bronchiectasis, and disease of the upper accessory air passages. They stated that in reviewing the literature they were unable to find any report of this condition written in the English language. They reported five such cases. The discussion of this paper indicated that the condition may be encountered and recognized more often than the literature implies. It is for this reason that this case is added.

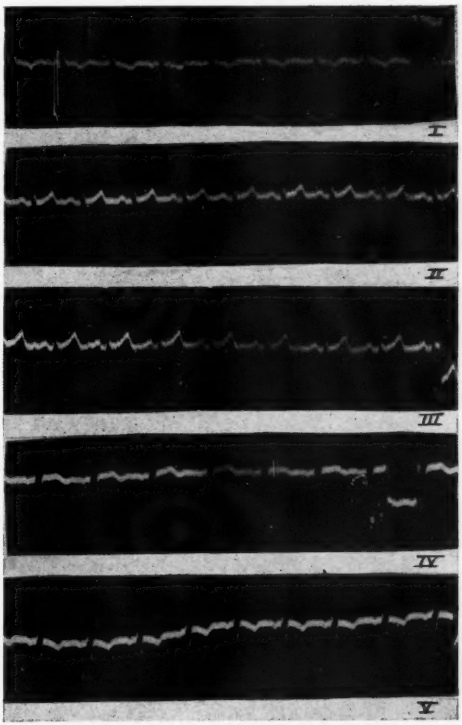

Fig. 1.—All complexes in Lead I are inverted. Lead IV was taken with the electrode over the true apex in the fifth intercostal space on the right. Lead V was taken with electrode at a corresponding point on the left side.

CASE REPORT

The patient was a white male, 22 years of age, who was complaining principally of dull headaches and impairment of hearing in the left ear. Since an early

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age he had had recurring attacks of bronchitis and a persistent upper respiratory infection. He had measles at the age of 2, and chicken pox and whooping cough before he was 10. At the age of 4 the tonsils and adenoids were removed, and this operation was repeated four years later. When he was about 9 years of age he

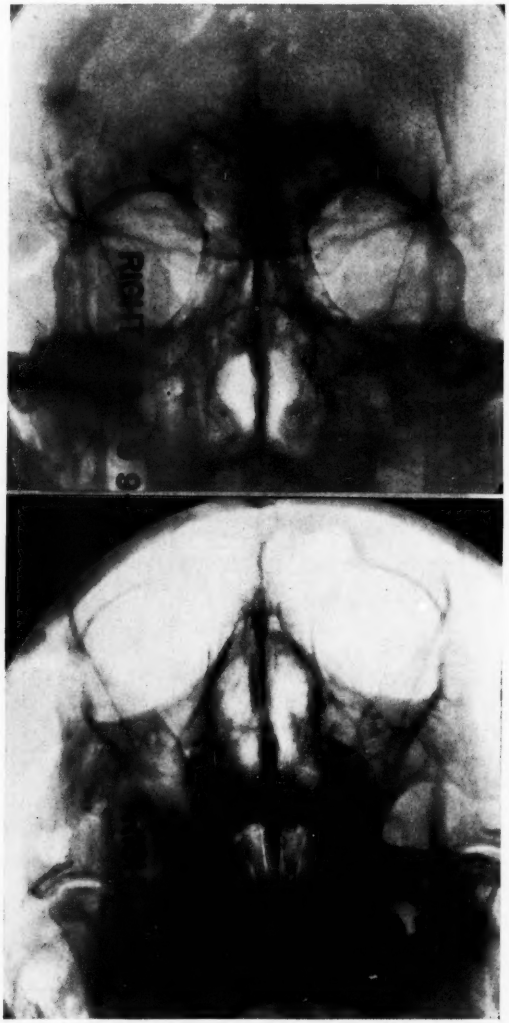

Fig. 2.

Fig. 3.

Figs. 2 and 3.—X-rays of sinuses showing a pansinusitis.

began having frequent headaches, and a definite diagnosis of sinusitis was made at this time. The antra were opened and drained. This was repeated in 1928 and again in 1930, with temporary relief of the headaches. Nasal polyps had been removed a number of times to facilitate nasal breathing. In 1930 he was given radium treatment in the nose without beneficial results. In 1936 a portion of the bone

was removed from the nose, and a short time following this, a radical antral operation was done on the right. In 1937 he had a series of x-ray treatments

Fig. 4.—X-ray of sinuses showing a pansinusitis.

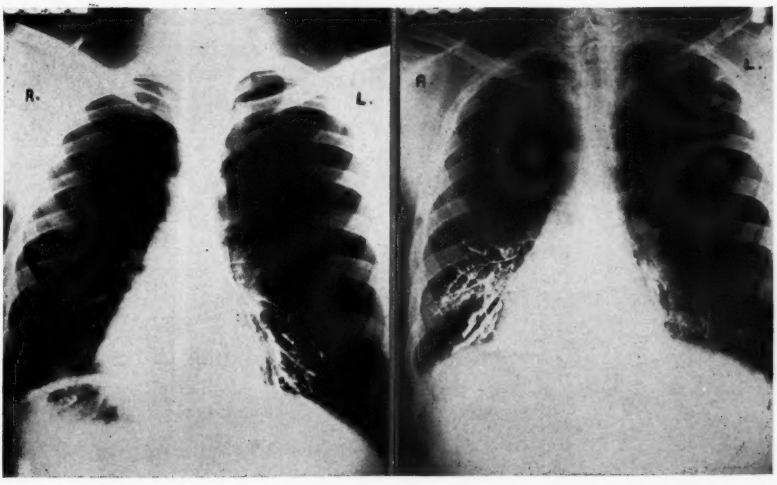

Fig. 5. Fig. 6.

Figs. 5 and 6.—Bronchograms showing a bilateral basal bronchiectasis. The heart and stomach are on the right side.

to the sinuses, which failed to produce much benefit. The operative procedures partially relieved the headaches, but the infection in his sinuses has persisted.

He has had no sense of smell for many years, and temporary partial deafness has frequently been present. He has had a chronic cough with expectoration since early childhood. In April of this year he had an acute pulmonary infection which apparently was an atypical pneumonia. He was given sulfanilamide at this time, and during the course of this treatment all the secretions from his sinuses disappeared and his sense of smell was normal. It was during this illness that he was told that his heart was on the right side. Following recovery from this illness the nasal drainage reappeared, and his sense of smell and hearing again became impaired. At the present time he is having dull headaches and partial deafness, as well as the usual drainage from his sinuses, and cough with expectoration.

Physical Examination.—The patient was a young white male of average size, weighing 135 pounds. The nasal mucosa was pale and swollen, and mucopurulent secretion was present in both nostrils. The heart was found on the right side. The maximal apex impulse was in the fifth right interspace, 9 cm. from the midsternal line. The pulse rate was 80, and the blood pressure, 118/72. The heart did not appear enlarged, and no murmurs were heard. Numerous sibilant râles were heard over both lungs and a number of moist râles were heard at the bases. The physical examination was otherwise normal.

Urinalysis and routine blood studies revealed nothing abnormal. The electrocardiogram showed inversion of all complexes in Lead I (Fig. 1). A roentgenologic diagnosis of pansinusitis had previously been made. The sinuses were x-rayed again, and there was still definite evidence of a pansinusitis (Figs. 2-4). X-ray examination of the lungs showed a thickening of the bronchi in both lower lobes, suggestive of bronchiectasis. The heart was on the right side. The stomach was on the right side, and it was assumed that the liver was on the left. Bronchograms were made after filling the lower lobe bronchi with lipiodol (Figs. 5 and 6). These revealed a definite cylindrical bronchiectasis in both lower lobes.

SUMMARY

The case is that of a 22-year-old white male who has situs inversus, pansinusitis, and bilateral basal bronchiectasis.

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Book Reviews

ARTIFICIAL PNEUMOTHORAX. ITS PRACTICAL APPLICATION IN THE TREATMENT OF PULMONARY TUBERCULOSIS. Contributions by Saranac Lake Physicians to the Studies of the Trudeau Foundation. Editorial Committee: Edward N. Packard, M.D., John N. Hayes, M.D., and Sidney F. Blanchet, M.D. Foreword by E. R. Baldwin, M.D. Illustrated with 85 engravings. Philadelphia, 1940, Lea & Febiger.

This book is the most recent addition to the Trudeau Foundation Studies. It includes, among other matters, a discussion of the physiology of artificial pneumothorax, the indications for and contraindications to its use, technique of the operation, complications to be expected and the results of treatment. There are also chapters on "Oleothorax" and "Thoracic Surgery in Relation to Artificial Pneumothorax." The book is based largely upon the wide experience of the contributors; it adequately covers the various aspects of the subject, presents the advantages, disadvantages, and limitations of the method, and is to be regarded as a reliable and conservative guide to the use of artificial pneumothorax. The book is highly recommended to physicians who are concerned in the treatment of patients with pulmonary tuberculosis.

Frederick T. Lord.

PRIMITIVE TUBERCULOSIS. By S. Lyle Cummins, C.B., C.M.G., LLD., M.D., Director of Research, Welsh National Memorial Association. 213 pages with 5 illustrations. London, 1939, John Bale Medical Publications, Ltd.

This is a book which seeks out pathways in the jungle of tuberculosis which are rarely trod upon by the great majority of physicians. Combining the resources of knowledge gleaned through his own extended studies and observations with those of numerous additional authors similarly well qualified to present soundly buttressed experiences and opinions, Dr. Cummins presents the problem of tuberculous infection among the primitive constituents of the human race. The author recognizes at the outset the difficulty inherent in any attempt to define exactly what constitutes a "primitive," yet he explains that his monograph deals particularly with the disease as it is found in the native populations of tropical and subtropical lands where European settlers have penetrated.

There are clear-cut descriptions of the acute, exudative, disseminate, and rapidly fatal infantile types of disease seen in all age groups among

these peoples. Observations made upon certain features of tuberculin testing in persons not protected by the relative safeguard of a tuberculous ancestry are unquestionably of considerable interest. It is one conclusion of the author, and well founded it appears to be, that for "primitive" people, "with civilization comes tuberculosis."

The monograph is well written and reveals evidence of care in assembling the material presented. It should be of especial interest to those physicians particularly concerned with tuberculosis as a disease, to epidemiologists, and certainly to anyone undertaking the practice of medicine among members of "primitive" races, whether as a unit of a medical mission, a governmental appointee, or by virtue of any other circumstance.

Edward M. Kent.

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